ABSTRACTS OF WORLD MEDICINE

VOL. 26 NO. 1 JULY, 1959

Pathology

1. Experimental Production of Carcinoma with Tobacco Products. V. Carcinoma Induction in Mice with Cigar, Pipe, and All-tobacco Cigarette Tar

A. B. CRONINGER, E. A. GRAHAM, and E. L. WYNDER. *Cancer Research* [*Cancer Res.*] **18**, 1263–1271, Dec., 1958. 11 refs.

A comparison of the carcinogenic activity of condensates of the smoke from cigars, pipe tobacco, cigarettes, and cigarette tobacco was made by painting them 3 times a week on the shaved skin of the backs of CAF_1 and Swiss mice. Tars from pipe tobacco and cigars were slightly more active than cigarette tar, while tar from all-tobacco cigarettes showed a lower activity than that from ordinary cigarettes. Dilution of the tars accelerated tumour formation. *G. Calcutt*

HAEMATOLOGY

2. The Clinical Significance of Lymphoreticular Types of Cell in the Blood. (Die klinische Beurteilung der lymphoretikulären Zellformen im Blut)

P. SCHARENBERG. *Deutsche medizinische Wochenschrift* [*Dtsch. med. Wschr.*] **83**, 2296–2298, Dec. 19, 1958. 30 refs.

Atypical mononuclear leucocytes, variously described as atypical lymphocytes, monocytes, or plasma cells, lymphoid, monocytoid, or lympho-monocytic cells, lymphatic irritative forms, or blast cells, occur in the blood during the acute phase of many diseases, especially virus infections. They resemble large lymphocytes or monocytes, with a round or kidney-shaped eccentric nucleus of loose granular texture and a deeply basophilic cytoplasm, frequently vacuolated. They are generally considered to arise from the lympho-reticular tissues (lymph nodes, spleen, liver, and bone marrow), the reaction of these tissues to the disease resulting in the release of immature forms into the peripheral blood. The atypical cells may be associated with either leucocytosis or leucopenia and may be preceded by neutrophilia with a shift of the Arneth count to the left.

Of the diseases in which these cells occur, infectious mononucleosis is the outstanding example, but they may also be found, though not in such large numbers, in infective hepatitis, rubeola, variola, virus pneumonia, influenza, mumps, whooping cough, ulcerative stomatitis, and many allergic conditions, and in blood diseases such as agranulocytosis, aplastic anaemia, and reticuloses. Such cells have also been observed by the author in one case of typhoid fever, one of tuberculous meningitis in its early stages, and one of osteomyelofibrosis. They are most readily demonstrated by centrifuging citrated blood and staining a smear of the leucocyte layer with May–Grünwald–Giemsa stain. Although they are not specific to virus infections their detection may be a valuable aid to the diagnosis of such diseases, and especially in the differentiation of epidemic hepatitis from chronic hepatitis, cirrhosis, and cholangitis of non-viral origin. *Ethel Browning*

3. A Study of Antigens of Human Leukocytes. [In English]

S.-Å. KILLMANN. *Vox sanguinis* [*Vox Sang. (Basel)*] **3**, 409–425, Dec., 1958. 22 refs.

The antigenic structure of human leucocytes was investigated by the author at Rigshospitalet, Copenhagen. Using sera only from patients who had received transfusions by a modification of Dausset's technique, he demonstrated by means of absorption and elution tests that: (1) leucocytes contain antigens which are not present in erythrocytes; (2) leucocytes contain at least four antigens, some being very common; (3) the presence of the leucocyte antigens is apparently not determined by a single pair of allelic genes; (4) leucocyte agglutinins can be of mixed specificity; and (5) normal leucocytes, leukaemic lymphocytes, and leukaemic granulocytes have antigens in common.

The possible role of leucocyte antigens in tissue transplantation is mentioned. *I. Dunsford*

4. Determination of Plasma-volume Using Intravenous Iron Dextran

A. MACKENZIE and J. TINDLE. *Lancet* [*Lancet*] **1**, 333–335, Feb. 14, 1959. 10 refs.

From the General Hospital, Sunderland, the authors describe the use of intravenous injections of iron–dextran complex (" imferon ") for the rapid and accurate estimation of plasma volume. A 5-ml. sample of blood is first removed from an arm vein; this can be allowed to clot or can be treated with heparin or oxalate (but not with " sequestrene "). Through the same needle 1 ml. of imferon (containing 50 mg. of elemental iron) is injected slowly by means of a tuberculin syringe with a to-and-fro movement of the plunger. After 15 minutes 5 ml. of blood is removed from the other arm. The circulating iron in both specimens is estimated by a simplified modification of the method described by Trinder (*J. clin. Path.*, 1956, **9**, 170), the centrifuge tubes used being

of hard glass and rendered iron-free by any of the accepted methods. In 6 experiments carried out on pooled plasma to which known amounts of imferon (500 to 2,500 μg. of iron per 100 ml.) had been added recovery was between 99 and 102%. When 18 subjects were given 1 ml. of imferon intravenously subsequent estimation of the plasma iron level showed that an average of less than 10% of the iron was lost from the circulation in 2 hours, a result similar to that obtained with azovan (Evans) blue. After 48 hours the level of iron in the circulation had decreased by 70 to 90%. Thus the estimation of plasma volume by this method can be repeated accurately within 48 hours of the injection of imferon.

In 12 healthy adults the plasma volume was estimated first by the imferon method and again 7 to 14 days later by the azovan blue method. The difference between the former and the latter result in 8 cases varied from +100 to −210 ml. In the remaining 4 subjects the difference was greater than this, but on repetition in 3 of them comparable figures were obtained, the results by the imferon technique remaining unaltered. (The fourth subject was not available for repetition.) It is considered that the original discrepancy in these cases was due to slight lipaemia causing inaccuracy of the azovan blue method.

The intravenous injection of 1 ml. of imferon results in a concentration of between 1,500 and 2,000 μg. of iron per 100 ml. of plasma. The accurate estimation of such levels is technically simple, requiring only 0·5 ml. of plasma and taking about 30 minutes. Imferon is neutral, isotonic, non-irritant, and of constant iron content. The estimation of plasma volume by this method is not affected by lipaemia; the only precautions necessary are the avoidance of haemolysis and the use of iron-free, hard glass tubes for the chemical estimations.

G. Clayton

5. **Egg-containing Meals and Blood Coagulation**
E. Orma, D. N. Rhodes, and A. Keys. *Lancet* [*Lancet*] **1**, 388–390, Feb. 21, 1959. 15 refs.

It is known that ingestion of a test meal containing two eggs is followed by a shortening of the one-stage clotting time of recalcified plasma when Russell viper venom is the source of thromboplastin (" stypven " time). Egg lipid contains neutral fat and phospholipid. There are two main phospholipids present—phosphatidyl choline and phosphatidyl ethanolamine. The object of the present study, carried out at the Hastings State Hospital, Minnesota, was to determine whether either of the two main phospholipids was responsible for the change in the stypven time. A whole-blood coagulation-time technique in siliconed tubes was also used. The meals tested contained carbohydrate with protein, egg-white, whole egg, total lipid, phosphatidyl ethanolamine-free lipid, and phospholipid-free lipid. [The original paper should be consulted for further technical details.]

It was found that total lipid shortens the stypven time. Removal of the total phospholipid or of the phosphatidyl ethanolamine from the total egg lipid did not significantly alter the shortening effect on the stypven time. With the amount of egg lipid used (from 3 eggs), the whole-blood coagulation time in siliconed tubes was not altered. *A. S. Douglas*

6. **A Critical Review of Human Haemoglobin Variants. Part I: Methods for Separation and Characterization; Part II: Individual Haemoglobins**
G. H. Beaven and W. B. Gratzer. *Journal of Clinical Pathology* [*J. clin. Path.*] **12**, 1–24, Jan., 1959; 101–115, March, 1959. Bibliography.

MORBID ANATOMY AND CYTOLOGY

7. **The Morphologic Elements in the Early Lesions of Arteriosclerosis**
H. Z. Movat, M. D. Haust, and R. H. More. *American Journal of Pathology* [*Amer. J. Path.*] **35**, 93–101, Jan.–Feb., 1959. 14 figs., 20 refs.

The structure of lesions which appeared to represent the earliest changes in the development of arteriosclerosis was studied in the Department of Pathology of Queen's University, Ontario, in a series of 148 aortas selected on the basis of the gross appearance. The lesions appeared as: (1) gelatinous elevations, (2) fatty dots and streaks, (3) small red mural thrombi, and (4) white opaque elevations (plaques). The findings in the first three groups are described; the fourth group is to be the subject of a later paper.

(1) Gelatinous elevations were circumscribed or diffuse and consisted of an oedematous swelling of the intima due to " insudation " of serum or plasma with and without lipids. The fat was present extra- or intracellularly.

(2) Fatty dots and streaks consisted of accumulations of foam cells located beneath the endothelium or deeper in the intima. There was no increase in connective tissue or reactive fibrosis in response to the deposition of lipids.

(3) Small red mural thrombi were composed of fibrin and platelets; occasionally some other constituents of the blood such as erythrocytes could be demonstrated. Very small fibrin thrombi were also found; these were visible microscopically only.

From these observations the authors conclude that the early focal lesions of arteriosclerosis in the aortic intima have at least three distinct patterns in their structural and chemical composition, but that it is not possible to determine " whether further evolutions of these lesions may lead to a common end stage ". *A. W. H. Foxell*

8. **Mast Cells in Human Tumors**
E. F. Lascano. *Cancer* [*Cancer* (*Philad.*)] **11**, 1110–1114, Nov.–Dec., 1958. 2 figs., 45 refs.

At the Institute of Surgery, Buenos Aires, the numbers of mast cells in histological specimens of different benign and malignant human tumours were compared with those in the normal tissues in which the tumour had formed. All material was fixed in formalin and stained with a variation of Unna's polychrome methylene blue. In general, the number of mast cells in benign tumours was lower than that in the corresponding normal tissue,

but occasionally, as in pigmented naevus, it was equal to or higher than in the normal tissue. Malignant tumours always contained many fewer mast cells than did normal tissue, with the sole exception of basal-cell carcinoma. The stroma of tumours, especially of malignant growths, is thus an unfavourable field for the development of mast cells. On the other hand increased numbers of mast cells are often found at the periphery of carcinomata. The author was unable to draw any definite conclusion concerning the function of mast cells in relation to tumours. *R. Wyburn-Mason*

9. **The Problems of Histological Diagnosis in Baso-squamous Cell Carcinoma of the Skin**
J. BURSTON and R. D. CLAY. *Journal of Clinical Pathology* [*J. clin. Path.*] **12**, 73–79, Jan., 1959. 6 figs., 27 refs.

For some time it has been held that baso-squamous-celled carcinoma of the skin is a distinct entity, intermediate in behaviour and histology between rodent ulcer and squamous-celled carcinoma and markedly more radioresistant than rodent ulcer; this view, however, has recently been questioned. The authors of this paper from the Portsmouth and Isle of Wight Area Pathological Service have reviewed a series of 28 cases in which baso-squamous-celled carcinoma was diagnosed on the basis of the skin biopsy findings. A critical reassessment of these findings showed that a diagnosis of baso-squamous-celled carcinoma could be substantiated in one instance only, and even this might have been a case of contiguous tumours. Excision biopsy had been carried out in this case 15 months previously, and at the time of the review there was no evidence of recurrence or metastasis. Follow-up investigation in the remaining cases did not reveal any unusual behaviour. The authors state that the principal source of error is the occurrence of areas of squamous differentiation in rodent ulcers, a common finding of no prognostic significance. *Bernard Lennox*

10. **Squamous Metaplasia of the Respiratory Tract Epithelium. An Autopsy Study of 214 Cases. 4. Relation to Bronchial Carcinoma.** [In English]
K. SANDERUD. *Acta pathologica et microbiologica Scandinavica* [*Acta path. microbiol. scand.*] **44**, 329–344, 1958. 11 figs., 43 refs.

The author compares the anatomical, age, and sex distribution of squamous metaplasia of the bronchial mucosa found at necropsy in 70 out of 214 unselected subjects studied at the Gade Institute, University of Bergen (*Acta path. microbiol. scand.*, 1958, **42**, 247, **43**, 47, and **44**, 21; *Abstr. Wld Med.*, 1958, **24**, 163 and 400, and 1959, **25**, 151), with the distribution of bronchial carcinoma in 3 large series reported by other authors. In both sexes squamous metaplasia was observed most frequently in those areas where carcinoma most commonly occurs, but it showed a far wider anatomical and age distribution, occurring in sites where cancer is but seldom found, such as trachea and carina, and being present in very young subjects. The age distribution of the more pronounced cases of metaplasia (Grade III in the author's classification) was, however, comparable to that of patients suffering from bronchial carcinoma. In no case was transition from metaplasia to carcinoma observed. *R. Salm*

11. **Squamous Metaplasia of the Respiratory Tract Epithelium. 5. A Contribution of the Pathogenesis of Metaplasia. Two Experimental Studies.** [In English]
K. SANDERUD. *Acta pathologica et microbiologica Scandinavica* [*Acta path. microbiol. scand.*] **44**, 345–362, 1958. 10 figs., 30 refs.

The author reports the results of experimental investigations into the possibility that squamous metaplasia of the respiratory epithelium may be due to a factor with a general effect on epithelial growth, as suggested by the frequent occurrence of metaplasia in the renal pelvis in uraemia, or that it occurs in the course of regeneration after local damage. In rats made uraemic by constriction of the hilus of one or both kidneys no squamous metaplasia was observed in the bronchial tree, though it was marked in the renal pelvis where, however, mechanical factors played a part. In rabbits in which the tracheal mucosa was incised and cauterized it was found that in the course of healing an acanthotic squamous plaque was formed which tended to persist for at least 6 weeks. The longest period of observation being 49 days, it was impossible to exclude the possibility that in some cases squamous metaplasia persists after injuries. The possible relation of these findings to the occurrence of squamous metaplasia in the human respiratory tract is discussed. *R. Salm*

12. **Congenital Pulmonary Lymphangiectasis**
K. M. LAURENCE. *Journal of Clinical Pathology* [*J. clin. Path.*] **12**, 62–69, Jan., 1959. 11 figs., 17 refs.

The author has already described the pathological features in 3 cases of congenital pulmonary lymphangiectasis (*J. Path. Bact.*, 1955, **70**, 325); in this paper from the Department of Morbid Anatomy, Portsmouth and Isle of Wight Pathological Service, he describes the findings in 7 further cases.

The lungs are usually bulky and inelastic, with pronounced lobulation. The subpleural lymphatic vessels are prominent and there are often subpleural cysts up to 3 mm. in diameter. Section of the lung shows a parenchyma diffusely honeycombed with cysts of irregular shape and size, up to 5 mm. diameter, and considerable increase in the fibrous tissue of the interlobular septa. In all the cases in the present series both lungs were uniformly affected by the cystic changes.

Histologically, the cysts are seen to be mostly in the subpleural and interlobular connective tissue, or closely related to bronchi and blood vessels. The cyst walls, rarely more than 10 μ in thickness, consist of a delicate network of elastin, collagen, and occasionally smooth muscle fibres. They are lined by a single layer of flat endothelial cells. Serial sections show the cystic spaces to be part of an intricate network of intercommunicating channels.

The author states that the position of the cystic spaces in the normal distribution of lymphatics, their close

relationship to blood vessels and bronchi, and their structures leave " little doubt that they must be derived from lymphatic vessels ". As the condition appears to be found only in stillborn infants and neonates it can be assumed to be congenital. The author suggests that it is possibly due to a continued growth of the lungs with a persistence of the amounts of connective tissue and lymphatics on the one hand and of lung tissue proper on the other in the proportions that exist normally in the 16th week of intra-uterine life. *H. Caplan*

13. **The Incidence Found at Necropsy of Metastases to the Sternum and Iliac Crest, with Special Reference to Carcinoma of the Lung**
M. O. SKELTON. *Journal of Clinical Pathology* [*J. clin. Path.*] **12**, 70–72, Jan., 1959. 3 refs.

At necropsy at Lewisham Hospital, London, on 225 unselected cases of malignant neoplasm metastatic malignant cells were found in the sternum or iliac crest, or in both, in 45 cases (20%). Metastases were present in 24 out of 69 cases of carcinoma of lung. It was noted that the oat-cell type of carcinoma was not only very liable to metastasize to the sternum (14 out of 26 cases), but was also likely to produce extensive replacement of the sternal marrow by tumour tissue. Of 9 cases of oat-cell carcinoma in which the duration of the disease was 6 weeks or less, the bone marrow was found to be almost completely replaced by malignant tissue in 5. The author suggests that " in suspected cases of carcinoma of the lung sternal puncture may be of value as a diagnostic procedure for the detection of malignant cells even when the clinical history is relatively short " and that sternal puncture is a justifiable preliminary procedure to thoracic surgery.

The number of cases of other forms of malignant disease with metastases to the sternum was too small to justify statistical appraisal, but the stomach, breast, prostate, and kidney were the chief primary sites. Metastases were discovered in 5 out of 37 cases of carcinoma of the stomach, confirming that this neoplasm tends to metastasize to bone, a fact which is not widely appreciated. *H. Caplan*

14. **Histological Changes in the Lung in Diseases Associated with Pulmonary Venous Hypertension**
D. HEATH and J. E. EDWARDS. *British Journal of Diseases of the Chest* [*Brit. J. Dis. Chest*] **53**, 8–18, Jan., 1959. 3 figs., 12 refs.

The histological changes in the lung in diseases associated with pulmonary venous hypertension were studied at the Mayo Clinic in three groups of patients. Group 1 contained 6 patients who had congenital heart diseases, without cardiac septal defects, which resulted in pulmonary venous and arterial hypertension. Group 2 consisted of 3 patients who had mitral atresia with a narrowly patent foramen ovale and a single ventricle with transposition of the great vessels. The authors state that while these patients had pulmonary venous hypertension from birth, the associated pulmonary arterial hypertension must be regarded as due to the free communication between the common ventricle and the lesser circulation. Group 3 contained 4 patients in whom pulmonary hypertension developed in adult life as a result of acquired non-rheumatic mitral incompetence (3 cases) or granuloma of the mediastinum constricting pulmonary veins (1 case).

In Groups 1 and 2 the elastic fibrils in the pulmonary trunk were long and regular, similar to those in the adult aorta, and showed little tendency to branching or fragmentation; they were tightly packed and tended to run parallel to one another. In Group 3 the arrangement of the elastic fibrils was that seen in the normal adult; the fibrils were short, fragmented, irregular, loosely and haphazardly arranged, and with a tendency to branching. The small pulmonary arteries in all cases showed various grades of hypertensive vascular disease with medial hypertrophy and cellular intimal proliferation or acellular intimal fibrosis.

Changes were found in the pulmonary veins in 10 cases in the series. Pulmonary veins more than 200 microns in diameter were thickened, the wall being composed of " tightly packed, circularly arranged, smooth muscle fibres, sandwiched between prominent internal and external elastic laminae ". Internal to this media was a thick layer of cellular fibrous tissue which contained fusiform cells scattered between the collagen fibres. Most of the venules (100 microns in diameter) showed severe intimal fibrosis, usually acellular but cellular in a few. The intimal fibrosis was more pronounced in adults with acquired pulmonary venous hypertension than in children with congenital pulmonary venous hypertension. There were no thrombi in the veins.

In all three groups of patients extensive changes were observed in the lung substance. In the lower lobes the alveoli contained oedema coagulum, macrophages, and erythrocytes. Much of the oedema coagulum had been organized by cellular fibrous tissue so that the alveolar space contained collagen in many instances. The alveolar walls were grossly thickened; this was due in part to distension of alveolar capillaries and in part to pulmonary interstitial fibrosis. At a late stage the affected lungs were solid with intra-alveolar fibrosis, chronic pulmonary interstitial fibrosis, and haemosiderin-laden macrophages. These changes were not found in the upper lobes or, if present, were less severe than in the lower lobes. Spicules of bone were found in the lungs of 2 adults.

The changes in the lung substance are considered to be " characteristic of, but not pathognomonic of, pulmonary hypertension since they occur in other conditions, including pulmonary infarction ". *H. Caplan*

15. **A Postmortem Analysis of 812 Gastroduodenal Ulcers Found in 20,000 Consecutive Autopsies, with Emphasis on Associated Endocrine Disease**
E. H. ELLISON, J. S. ABRAMS, and D. J. SMITH. *American Journal of Surgery* [*Amer. J. Surg.*] **97**, 17–30, Jan., 1959. Bibliography.

Some recent observations have indicated that there may be more than a casual relationship between the endocrine system and acid-peptic disease. The authors

therefore examined the records at the Ohio State University Health Center, Columbus, of 20,000 consecutive necropsies performed between 1937 and 1955. A total of 812 cases of active gastroduodenal ulceration were found, an incidence of 4·1%. The ulcers were classified as follows: chronic duodenal 232 (28·5%), acute gastric 230 (28·3%), acute duodenal 157 (19·5%), chronic gastric 142 (17·4%), combined chronic duodenal and gastric 23 (2·8%), combined acute duodenal and gastric 21 (2·6%), and stomal 7 (0·9%). Males were affected at least twice as often as females with all types of ulceration. Only 2·7% of the cases of chronic ulcer were in patients under 30, while 7% of all cases of ulceration occurred in the aged, despite the reported high incidence of achlorhydria in this age group. In nearly half of the patients death was attributable to the ulceration.

Chronic ulcers were usually larger than acute ulcers, and in about 20% of the patients they were multiple. Most gastric ulcers, acute and chronic, were on the lesser curve within 5 cm. of the pylorus. About 6% of chronic duodenal ulcers were in the second part of the duodenum. About one in every 10 patients with gastroduodenal ulceration had associated oesophageal ulceration. Concomitant central nervous system disease was found in 37% of patients with acute and 7% of patients with chronic gastroduodenal ulcer. Adrenal cortical hyperplasia was twice as common in patients with ulcer as in those without, but, with the exception of the rare islet-cell abnormalities of the pancreas, there was no morphological evidence to suggest that other endocrine glands had an aetiological relationship. *A. Wynn Williams*

16. **The Glomerular Lesions of Diabetes Mellitus and Their Electron-microscope Appearances**

A. BERGSTRAND and H. BUCHT. *Journal of Pathology and Bacteriology* [*J. Path. Bact.*] 77, 231–242, 1959. 11 figs., bibliography.

In this paper from the Department of Pathology of the Karolinska Institute, Stockholm, the authors describe the electron-microscopic appearances of the renal glomeruli in 8 patients with diabetes of 7 to 29 years' duration and attempt to correlate the morphological changes observed with the results of studies of renal function. Renal biopsy specimens were obtained from each patient (in 2 cases during adrenalectomy) and in one case the kidneys were also studied post mortem.

All the specimens showed the typical lesions of diabetic glomerulosclerosis, consisting in (1) diffuse lesions, shown by electron-microscopy to be due to thickening of the basement membrane, and (2) nodular lesions, which were shown to be hyaline masses precipitated in the endothelial cells. The renal function tests, which included determination of urinary protein excretion, serum non-protein nitrogen level, inulin clearance, renal plasma flow, and filtration fraction, showed that a minimal impairment of renal function was associated with mild diffuse changes in the glomeruli, whereas severe renal damage was associated with the presence of large globular hyaline masses in the glomerular capillaries. In discussing the nature of these changes the authors state that the great thickening of the basement membrane found in the diffuse lesions is assumed to be a metabolic change, " possibly a depolymerization of the polysaccharides ". The hyalinization of the endothelial cells (globular lesions) was found to start in the basement membrane close to the endothelial-cell membrane, but the authors are uncertain " whether the basement-membrane and endothelial-cell changes are parts of the same metabolic alteration affecting the mucoproteins or whether they are two processes differing to some degree both chemically and morphologically ". The composition of the hyaline substance is unknown; fine fibrils lying close to the endothelial-cell membrane were demonstrated in it in one case.

The great thickening of the basement membrane is considered to account for the decreased filtration rate and lowered filtration fraction in the diabetic kidney. The apparent paradox of concomitant proteinuria is explained by postulating that the basement membrane is a gel which has fine " pores " for " sieving " the proteins and that for some reason the size of these pores is increased in diabetes. *I. Berkinshaw-Smith*

17. **Pathological Findings in Jaundice Associated with Iproniazid Therapy**

H. POPPER. *Journal of the American Medical Association* [*J. Amer. med. Ass.*] **168**, 2235–2242, Dec. 27, 1958. 4 figs., 17 refs.

Iproniazid phosphate, an amine oxidase inhibitor, has been used in the treatment of tuberculosis and, more recently, in alleviating various mental disorders. Since a number of workers have observed jaundice in patients given iproniazid therapy, the author, at the Mount Sinai Hospital, New York, studied the pathological features of liver tissue obtained at biopsy or necropsy from patients treated with this drug. The material consisted of 13 biopsy and 16 necropsy specimens from 27 patients who had received from 600 to 19,200 mg. of iproniazid over periods ranging from 4 to 126 days.

The pathological picture was that of a diffuse hepatic parenchymal disease which varied from a spotty necrosis of single cells to a diffuse massive necrosis and collapse, both associated with inflammatory infiltration. These morphological changes were indistinguishable from those considered typical of viral hepatitis. No evidence of pre-existing liver disease was found. The clinical manifestations were also those of a diffuse hepatic parenchymal disease. In contrast, however, to the usual clinical picture in viral hepatitis, fever was frequently absent, while jaundice was on the average deeper and the histological changes were more severe than would be expected from the clinical manifestations. Also, the process as a whole was more virulent and the mortality higher. No relationship was found between the dosage of iproniazid and the extent of the lesion, and jaundice appeared as late as 20 days after cessation of treatment with the drug.

The part played by iproniazid in producing these morphological changes is not clear, but the probability has to be considered that this drug may activate an existing subclinical viral hepatitis—for example, in a carrier of serum hepatitis. *A. W. H. Foxell*

Microbiology and Parasitology

18. **Preliminary Observations on the Cultivation and Morphology of a Microorganism from the Cerebrospinal Fluid of Patients with Multiple Sclerosis**
R. M. MYERSON, S. W. WOLFSON, and T. SALL. *American Journal of the Medical Sciences* [*Amer. J. med. Sci.*] **236**, 677–691, Dec., 1958. 15 figs., 44 refs.

In a preliminary attempt to isolate micro-organisms from the cerebrospinal fluid (C.S.F.) of patients with disseminated (multiple) sclerosis (D.S.) the authors, working at the Veterans Administration Hospital, Philadelphia, used thioglycollate medium prepared by Ichelson, who has recently reported the successful isolation of a spirochaete from the C.S.F. of 59 out of 76 patients with D.S. (*Proc. Soc. exp. Biol. (N.Y.)*, 1957, **95**, 57; *Abstr. Wld Med.*, 1958, **23**, 5). Mature growth of a spirochaete-like organism was successfully obtained from 2 out of 4 samples of C.S.F. from patients with moderately advanced D.S., but none from 7 samples from patients with other disease processes.

Encouraged by these findings they made further cultures in medium prepared in their own laboratory according to Ichelson's formula. With this medium they obtained growth after 3 weeks' anaerobic culture at 28 to 30° C. from the C.S.F. of 3 patients with typical D.S. Fluid from 2 further cases gave doubtful growth, while negative cultures were obtained with fluid from one definite, one probable, and 2 possible cases of D.S. and from 14 control cases.

The morphology of the organism, as seen by phase-contrast microscopy in the living state and electron microscopy after fixation, is described. The authors are convinced that it was neither an artefact nor a laboratory contaminant. They state that it appeared to be morphologically identical with the organism first described by Steiner and named by him *Spirochaeta myelophthora* and with that isolated by Ichelson and others. The difficulty of isolation and the poor growth of the organism they ascribe largely to inadequacy of the present medium. They make no claims concerning the possible aetiological role of the organism, but stress the necessity for further study. *J. B. Cavanagh*

19. **The Demonstration of Proteolytic Enzyme Activity of *Entamoeba histolytica* by the Use of Photographic Gelatin Film**
C. HARINASUTA and B. G. MAEGRAITH. *Annals of Tropical Medicine and Parasitology* [*Ann. trop. Med. Parasit.*] **52**, 508–515, Dec., 1958. 1 fig., 8 refs.

In experiments at the Liverpool School of Tropical Medicine it was found that the proteolytic activity of living *Entamoeba histolytica* could be demonstrated by placing a drop of a suspension of amoebae in saline on the gelatin surface of a piece of exposed and developed 36-mm. photographic film. After an hour's incubation at 37° C. the gelatin film under the drop had dissolved away, leaving a clear spot, whereas control drops of a suspension of associated bacteria and of saline on the same piece of film did not dissolve the gelatin. It was also demonstrated by this method that a saline extract of amoebae which had been disintegrated by freezing and thawing was proteolytic, the activity of the extract being observed at *p*H values ranging from 6·0 to 8·0 and being removed by filtration through a Seitz pad. The extract was stored for 14 days at −79° C. and for 7 days at 4° C. without loss of activity. The presence or absence of rice starch in the medium used for cultivation of the amoeba did not affect the degree of proteolysis. Horse serum inhibited the action of the enzyme on gelatin. *R. A. Neal*

20. **Studies on the Microscopic Slide-agglutination Test for Q Fever**
B. BABUDIERI. *Bulletin of the World Health Organization* [*Bull. Wld Hlth Org.*] **19**, 981–994, 1958. 21 refs.

A microscopic slide agglutination test for the serological diagnosis of Q fever was described by the author (with Secchi) in 1952 (*R.C. Ist. sup. Sanità*, **15**, 584). In the present paper from the laboratories of the California State Department of Public Health, Berkeley, he reports a comparison of the sensitivity of his test with that of the macroscopic or tube agglutination test, the capillary agglutination test, and the complement-fixation test and discusses the factors which may inhibit or enhance the agglutination reaction. The tests were carried out on the sera of 72 sheep infected with Q fever and the results are presented in tables. An index of the sensitivity of each test was obtained by multiplying the number of sera which reacted to each titre by the value of the titre and adding the products. On this basis the slide agglutination test was found to be about 23 times more sensitive than the complement-fixation test and about 10 times more sensitive than either of the other two agglutination methods.

The factors inhibiting agglutination are discussed, the author suggesting that complement or an allied substance may be responsible for inhibiting the reaction when fresh serum is used. Serum for use in the micro-agglutination test is therefore inactivated at 56° C. for 30 minutes. Tests on a human serum with a micro-agglutination titre of 1:64 showed that the sensitivity of the test was increased by the addition of fresh inactivated bovine serum (" auxi-agglutination ") or of fresh bovine serum and complement (" conglutination "). However, the author considers the unmodified test to be sufficiently sensitive for routine diagnostic or epidemiological studies, while any advantage offered by the modification is offset by the need for supplies of fresh bovine serum. The micro-agglutination technique is not only more sensitive than the other methods, but it also has the advantages that it requires less antigen and can be performed on dried blood, which is useful in large-scale studies. *I. Berkinshaw-Smith*

Pharmacology and Therapeutics

21. **The Use of Polosuhin's Anti-shock Fluid in the Treatment of Collapse Caused by Food Poisoning.** (Применение противошоковой жидкости Полосухина при коллапсе у больных пищевыми токсикоинфекциями)
D. M. Соц. *Терапевтическии Архив* [*Ter. Arh.*] **30**, 64–66, No. 12, Dec., 1958.

For the treatment of patients in collapse following acute food poisoning the author recommends the infusion of Polosuhin's fluid, which is a saline solution made up of 25 g. of sodium chloride, 0·5 g. of sodium hyposulphite, and 1·5 g. of calcium chloride in 500 ml. of distilled water, given intravenously over a period of not more than 15 to 18 minutes. In severe cases 500 ml. should be infused, but in milder cases 250 to 400 ml. may suffice. When the first infusion does not produce a satisfactory result a second may be given, preferably not less than 5 hours after the first. In all cases it is essential to carry out a thorough gastric lavage before starting the infusion.

In 27 out of 38 cases so treated by the author the patient's condition became satisfactory within 24 hours of giving the fluid; in the remaining 11 cases improvement was delayed until between the 3rd and 9th days.

A. Orley

22. **Clinical Experience with Lanatoside A.** (Klinische Erfahrungen mit dem Lanatosid A)
H. Thiesen. *Deutsche medizinische Wochenschrift* [*Dtsch. med. Wschr.*] **84**, 32–38, Jan. 2, 1959. 1 fig., 14 refs.

The clinical effects of "adigal", a preparation of lanatoside A, one of the three glycosides first isolated by Stoll from *Digitalis lanata* and chemically related to digitoxin, were studied in 90 cases of congestive heart failure of varying degree and aetiology at the Ochsenzoll General Hospital, Hamburg. Atrial fibrillation was present in 44 cases, with a high ventricular rate and pulse deficit in 28. Quantitative studies were carried out on this last group of 28 patients. Reduction of the ventricular rate was taken as a measure of the effective concentration of the glycoside in the blood, saturation being indicated by reduction of the ventricular rate to normal and disappearance of the pulse deficit. When medication was stopped it was found that the ventricular rate started to rise again when the concentration of the drug in the blood fell below 25% of the saturation level. On the basis of this observation the rate of dissipation and the maintenance dose could be calculated. With daily doses of 1·6 to 2 mg., given intravenously, generally in 2 injections, saturation was achieved within 3 to 5 (occasionally 7) days. For the group of 28 patients as a whole the average saturation dose was 3·88 mg.; for patients with moderately severe failure it was 4·21 mg. and for those with the most advanced degree of failure 5·12 mg. The maintenance dose was generally 0·4 mg. by mouth daily, but in about 25% of cases 0·6 to 0·8 mg. was needed. These doses are higher than those reported by others. Even in the absence of congestion absorption varied between 50 and 75% of the dose. The rate of dissipation of the drug was found to be 13% per day.

In 12 cases saturation was achieved with lanatoside A and treatment was then continued, with or without a day's interval, with intravenous injections of strophanthin (0·1 mg. daily for the first 2 or 3 days, the dose being subsequently gradually increased to 0·25 mg.) in order to avoid the uncertainty of absorption with oral administration. On the other hand in 62 cases lanatoside A was used for maintenance, either after intravenous strophanthin or squill medication or, in a few cases, without any previous treatment; the usual dose was 0·4 mg. a day.

The author concludes that lanatoside A is a reliable and well tolerated cardiac glycoside with a rate of dissipation intermediate between those of gitalin and lanatoside C, but with a far greater therapeutic margin, which is of particular value in patients prone to develop signs of intoxication. In some cases it appears preferable to lanatoside C.

A. Schott

23. **Relief of Post-operative Pain**
E. Cope and P. O. Jones. *British Medical Journal* [*Brit. med. J.*] **1**, 211–213, Jan. 24, 1959. 12 refs.

A comparative study is reported of the analgesic effects of papaveretum, dipipanone, dihydrocodeine, and dextromoramide in the relief of pain following severe gynaecological operations in a total of 390 patients. The drugs were administered subcutaneously every 6 hours for the first 36 hours after operation, the dose level chosen for each drug being that which would be expected to give a good level of analgesia with minimal side-effects—namely, papaveretum 20 mg., dipipanone 25 mg., dihydrocodeine 50 mg., and dextromoramide 10 mg. In producing analgesia dihydrocodeine was the least effective drug, the analgesic effect of the others being about equal. Vomiting occurred most frequently with dextromoramide and least frequently with dipipanone. Patients receiving papaveretum or dextromoramide were able to sleep at night without additional sedatives; patients receiving the other analgesics needed a barbiturate. The authors conclude that the order in which the four drugs satisfied the criteria of a good postoperative analgesic was dipipanone, papaveretum, dextromoramide, and dihydrocodeine.

V. J. Woolley

24. **Studies on Iron–Dextran Complex.** [Monograph, in English]
T. Karlefors and Å. Nordén. *Acta medica Scandinavica* [*Acta med. scand.*] **163**, Suppl. 342, 1–54, 1958. 26 figs., bibliography.

Chemotherapy

25. **Staphylococcal Resistance to Ristocetin, Oleandomycin, and Novobiocin**
JEN-YAH HSIE, W. NUSSER, S. EPSTEIN, H. VAN MARDEN, and S. OZOG. *Antibiotics and Chemotherapy* [*Antibiot. and Chemother.*] **8**, 607–614, Dec., 1958. 6 figs., 10 refs.

Conflicting reports have been published of the rate of development of resistance to ristocetin by staphylococci, as estimated by the serial-transfer method. Using the agar-plate technique, which they claim to be more efficient and to give more reproducible results than the serial-transfer technique, the present authors, working at the Still College of Osteopathy and Surgery, Des Moines, Iowa, were able to develop mutant strains of *Staphylococcus aureus* which showed resistance to ristocetin. Similarly, oleandomycin-resistant and novobiocin-resistant strains were isolated. The magnitude of the increase of resistance to ristocetin was small at each step, a five-fold increase of resistance requiring 10 steps. With novobiocin, however, a 1,100-fold increase of resistance required only 5 steps, while with oleandomycin a 1,000-fold increase required only 3 steps. Moreover, ristocetin-resistant strains reverted to lower grades of resistance more rapidly than those resistant to novobiocin and oleandomycin.

Of 98 strains of staphylococci recently isolated from clinical specimens, 6 were naturally resistant to novobiocin and 9 to oleandomycin. Neither these strains nor those with induced novobiocin or oleandomycin resistance showed any significant cross-resistance to penicillin, erythromycin, carbomycin, the tetracyclines, or chloramphenicol, nor were strains resistant to these last antibiotics significantly resistant to novobiocin or oleandomycin. *A. Ackroyd*

26. **The Use of Routine Antibiotic Sensitivity Tests in the Treatment of Various Infections**
S. HABERMAN. *Antibiotics and Chemotherapy* [*Antibiot. and Chemother.*] **8**, 615–626, Dec., 1958. 1 fig., 23 refs.

Tests of sensitivity to penicillin, bacitracin, dihydrostreptomycin, chlortetracycline, oxytetracycline, chloramphenicol, polymyxin B, and erythromycin were performed by the impregnated paper disk method as a routine on 294 micro-organisms isolated from 244 cases of infection at Baylor University Hospital, Dallas, Texas, between August, 1951, and September, 1953. Exceptions to the usually accepted pattern of susceptibility to the various antibiotics were observed quite frequently and it is concluded that " regardless of the source of infection, variation in sensitivity to antibiotics is more a function of the individual organism than the infection concerned ".

Of the broad-spectrum antibiotics, chloramphenicol was the most active, 81·6% of all strains being sensitive to it, followed by oxytetracycline (64·9%), chlortetracycline (64·3%), and dihydrostreptomycin (37·4%). Penicillin was effective against 55·6% of 106 strains of cocci and Gram-positive organisms, while 78·7% of 108 strains of cocci, diphtheroids, and *Haemophilus* were sensitive to bacitracin and 61·8% to erythromycin. The most frequently isolated organism was *Escherichia coli*, followed by *Staphylococcus aureus*.

A study of the outcome of treatment in relation to the results of sensitivity tests showed that prompt treatment with the antibiotic indicated by the test gave the best rate of recovery with least number of failures and no deaths. These findings confirm the value of antibiotic sensitivity testing by the impregnated disk technique as a guide to therapy. *A. Ackroyd*

27. **Demethylchlortetracycline: a Clinical Comparison of a New Antibiotic Compound with Chlortetracycline and Tetracycline**
W. M. SWEENEY, S. M. HARDY, A. C. DORNBUSH, and J. M. RUEGSEGGER. *Antibiotics and Chemotherapy* [*Antibiot. and Chemother.*] **9**, 13–22, Jan., 1959. 6 figs., 7 refs.

Demethylchlortetracycline, a new antibiotic, is much more stable than the tetracycline antibiotics now in clinical use. Likewise it has a high order of activity against bacterial test organisms. It is well absorbed from the human gastrointestinal tract and produces strikingly prolonged serum antibiotic concentration, probably due to its relatively slow excretion by the kidneys. This combination of chemical, pharmacological, and antimicrobial advantages suggests that demethylchlortetracycline merits trial in the treatment of sensitive microbial infections in man.—[Authors' summary.]

28. **Further Study on Griseoflavin. Identification with Novobiocin**
M. KUROYA, K. KATAGIRI, K. SATŌ, and M. MAYAMA. *Journal of Antibiotics* [*J. Antibiot.*] **11**, 187–192, Sept., 1958 [received Jan., 1959]. 3 figs., 8 refs.

The comparative experiment on griseoflavin and novobiocin indicated that both antibiotics were closely related in taxonomy, physico-chemical properties such as decomposition point, elemental analysis, ultraviolet and infrared spectra and papergrams, and also in antibacterial spectrum.

From the above-mentioned results, we considered that the griseoflavin is identical with the novobiocin.—[Authors' summary.]

29. **Body Fluid Concentrations of Penicillin following Intramuscular Injection of Single Doses of Benzathine Penicillin G and/or Procaine Penicillin G**
W. W. WRIGHT, H. WELCH, J. WILNER, and E. F. ROBERTS. *Antibiotic Medicine and Clinical Therapy* [*Antibiot. Med.*] **6**, 232–241, April, 1959. 6 refs.

Infectious Diseases

30. **Poliomyelitis: Virological Diagnosis and Immunological Studies.** (Sur la poliomyélite. Diagnostic virologique et études immunologiques)
R. DEBRÉ, V. DROUHET, and J. CELERS. *Bulletin de l'Académie nationale de médecine* [*Bull. Acad. nat. Méd. (Paris)*] **142**, 925–933, Dec. 16, 1958.

This is an account of some of the work of the virological laboratory established in Paris in 1954 for the study of poliomyelitis in association with the International Children's Centre. Of 311 specimens of stools from clinically confirmed cases, 288 were virologically positive; of the 23 negative specimens, 18 had been taken 10 days to 3 months after the beginning of the clinical illness. It is known that although the virus may persist in the stools exceptionally for more than 40 days from the onset of the disease, the quantity of virus present decreases rapidly after 7 to 10 days. When specimens taken after 10 or more days of illness were excluded the proportion from which the virus was isolated was 97% in 1954–6 and 99% in 1957. It is therefore concluded that virological confirmation of a clinical diagnosis of poliomyelitis is required only in exceptional cases, such as those of apparent upper motor neurone paralysis, lymphocytic meningitis, or meningo-encephalitis.

As an example of a different type of activity undertaken by the laboratory an account is given of a serological study carried out on children attending 2 schools situated 2 km. apart, at one of which 7 cases of Type-1 poliomyelitis had just occurred, while at the other no case of poliomyelitis had occurred for several years. The proportions of children in the 2 groups with neutralizing antibodies in the serum were, respectively: for Type 1 80% and 86%; for Type 2 64% and 65%; and for Type 3 66% and 70%. The highest proportion of children with Type-1 antibodies was found among those aged 5 years. This study indicates the high rate of diffusion of Type-1 strains of poliomyelitis virus and at the same time the diversity of their pathological action, since the clinical disease had occurred only at one school, whereas the antibody rate was of the same order in both populations. Rapidity of diffusion of a Type-1 strain was also demonstrated in a one-block children's hospital where, 10 days after the first clinical case of poliomyelitis appeared, 45 of the 91 patients were found to be carriers of Type-1 virus. The carrier state gradually regressed until, on the 83rd day, only 2 Type-1 carriers could be found. Yet 15 of the children remained free from poliomyelitis virus throughout.

Estimations of the serum antibody levels in children of similar socio-economic groups in different towns in France and in Dakar showed there to be considerable differences in the rate of acquisition of antibody to the 3 types. The most complete diffusion of infection was found after an outbreak of poliomyelitis in a village near Dakar, where the serum of every infant under one year of age was found to contain antibody to at least one type. In Dakar itself this standard was attained in children of about 3 years of age, and in the towns studied in France not until 15 years of age. *H. Stanley Banks*

31. **A Series of 170 Cases of Respiratory Poliomyelitis Treated at the Hôpital des Enfants-Malades, Paris, 1950–7.** (Sur 170 cas de poliomyélite respiratoire traités à l'hôpital des Enfants-Malades de 1950 à 1957)
M. S. THIEFFRY, C. MARTIN, and M. ARTHUIS. *Bulletin de l'Académie nationale de médecine* [*Bull. Acad. nat. Méd. (Paris)*] **142**, 933–941, Dec. 16, 1958.

In the classification of respiratory poliomyelitis it is of major importance to distinguish those cases in which respiratory difficulty is secondary to paralysis of swallowing, and therefore purely obstructive in nature, from those in which the difficulty is of pulmonary origin. In 57 cases of the former type admitted to the Hôpital des Enfants-Malades, Paris, during the 7 years 1950–7, treatment was relatively easy, mainly consisting in postural drainage, aspiration of respiratory secretions, and parenteral feeding. There were only 2 fatal cases, although 6 children required tracheotomy. Complete recovery of the power of swallowing almost invariably occurs, although the process is sometimes slow—in one case the disability lasted 18 months.

In cases of poliomyelitis with the other type of respiratory difficulty (of which 113 cases were admitted during the same period) the prognosis is much more serious. Two groups of cases may be distinguished: (*a*) those in which the difficulty is due to paralysis of the respiratory muscles only ("dry" type); and (*b*) those in which the respiratory muscular paralysis is complicated by paralysis of swallowing and resultant retention of secretions in the bronchi ("wet" type). A striking contrast is drawn between the results of treatment in the 41 cases (including both "dry" and "wet" types) admitted during the years 1950–5, and the 72 cases admitted in 1956 and 1957, when tracheotomy and positive-pressure respiration were freely used. Whereas in the former period the mortality was 58% (24 deaths), in the latter it was only 24% (17 deaths). Of the 72 survivors, after a minimum follow-up period of 9 months 66 had complete respiratory autonomy and only 6 were still dependent, for part of the day at least, on respirators.

The achievement of such results demands an organization which can ensure early diagnosis, immediate and "safe" transport to hospital (that is, with facilities for the treatment of respiratory obstruction and insufficiency *en route*), and treatment in a special centre thoroughly equipped with respirators of all kinds and with a trained medical, nursing, and engineering staff. The mechanical equipment in such a centre is indeed indispensable, but the heaviest responsibility lies not on

the engineering staff, but on the doctor, who must decide the type of treatment required at each stage, and at times also on the nursing staff, on whom may depend the prompt application of life-saving measures in emergencies. *H. Stanley Banks*

32. **The Antibiotic Prophylaxis of Bacterial Complications of Measles**
S. KARELITZ and H. D. ISENBERG. *Journal of Pediatrics* [*J. Pediat.*] **54**, 1–10, Jan., 1959. 2 figs., 14 refs.

During the 3 years 1956–8 251 patients with measles were observed by the authors—173 at home and 78 at Queens General Hospital, New York. Antibiotics were given prophylactically to 88 of the former and to 26 of the latter group, the drugs most commonly used being penicillin and erythromycin. In the domiciliary group, 15·9% of those receiving prophylactic treatment developed complications (bronchitis, pneumonia, or otitis media), while in the hospital group the proportion was 8%. The corresponding figures for those patients who received no prophylactic drugs were 21·2% and 32%. The authors ascribe the differences between the groups treated at home and in hospital to differences in age and socio-economic conditions, the latter being worse in the hospital patients. There was no evidence of development of bacterial resistance or of superinfection, this being ascribed to the fact that the prophylactic drugs were given neither in large doses nor for long periods. The distribution of the usual nasopharyngeal pathogens did not vary appreciably between the various groups. Although they condemn the indiscriminate use of antibiotic prophylaxis rather than gamma globulin in measles, the authors consider that the former should be used for infants under 3 years old, older individuals [age not specified], pregnant women, and children or adults already ill with serious cardio-respiratory complications. *I. M. Librach*

33. **The Treatment of Whooping Cough with Placental Gamma Globulin.** (Лечение коклюша плацентарным гамма-глобулином)
K. S. LADODO and S. N. BAVAEVA. *Педиатрия* [*Pediatrija*] **36**, 38–42, Feb., 1959. 4 refs.

In 200 samples of placental gamma globulin, agglutinins against *Haemophilus pertussis* were present in titres of 1:320 to 1:800. Placental gamma globulin was used in the treatment of 38 children with whooping cough, 3 doses of 3 to 6 g. being injected intramuscularly at intervals of 48 hours. There were 24 children under 6 months old, 7 between 6 and 12 months, and 7 between 1 and 3 years. In 4 cases the disease was mild, in 14 moderate, and in 17 severe. Antibiotics were given when indicated.

Of the 38 children treated, the gamma globulin definitely improved the condition of 28 and had no effect on 10. Signs of improvement were first noticed 3 to 4 days after the first injection and included a diminution in lymphocytosis and leucocytosis. Reactions to the administration of gamma globulin were insignificant. The earlier the treatment is started, the better the effect. *H. W. Swann*

34. **Experience with Amphotericin B for the Treatment of Systemic Mycoses**
J. H. SEABURY and H. E. DASCOMB. *A.M.A. Archives of Internal Medicine* [*A.M.A. Arch. intern. Med.*] **102**, 960–976, Dec., 1958. 1 fig., 7 refs.

Amphotericin B, an antibiotic produced by a species of *Streptomyces*, has no antibacterial properties, but is very active against fungi which produce systemic mycoses in man. It is relatively insoluble and is therefore given in the form of a colloidal suspension, intravenous injection being the best method of administration. The incidence of toxic reactions is high, especially at the beginning of treatment, but the severity of these reactions is reduced by the addition of the sodium succinate ester of hydrocortisone.

Of 4 patients with histoplasmosis, 3 who were given amphotericin B intravenously responded completely, while one who was given the antibiotic by mouth did not benefit. A satisfactory response was obtained in 5 patients with blastomycosis, although one died from staphylococcal septicaemia, the lung tissue in this case being negative for *Blastomyces*. Of 7 patients with cryptococcosis of the central nervous system, which is usually fatal, 5 responded satisfactorily, although 3 were acutely ill. Amphotericin B was also tried in patients with moniliasis, coccidioidomycosis, and sporotrichosis, but the results were inconstant and there were too few cases for adequate evaluation of the drug. *Winston Turner*

35. **Treatment of Trichuriasis with Dithiazanine. A Preliminary Report**
D. H. D. PAINE, E. S. LOWER, and T. V. COOPER. *British Medical Journal* [*Brit. med. J.*] **1**, 93–95, Jan. 10, 1959. 1 fig., 11 refs.

Dithiazanine was given in the treatment of trichuriasis in 6 mentally deficient patients at Coldharbour Hospital, Sherborne, Dorset. The ages of the patients ranged from 14 to 20 years and body weight from 30 to 64 kg. Preliminary egg counts made by a dilution technique showed that the infections were relatively light, the number of eggs per gramme of faeces ranging from 400 to 8,100. The drug was given in a dosage of 200 mg. 3 times a day for 5 successive days, regardless of the age or weight of the patient. Faeces were examined by dilution count immediately after completion of treatment. None of the patients had ova of *Trichuris* in the faeces at the first post-treatment examination. After an interval of one month faecal specimens were examined by De Rivas's concentration technique. Scanty ova were found in the specimens from one patient only; as this patient had persistently chewed the tablets of dithiazanine and vomited on 3 of the 5 treatment days it appeared likely that he had not received the full dose.

Side-effects of the drug were minimal; 3 of the 6 patients vomited, and in 2 of these and one other patient there was a transient rise in pulse rate and temperature. No side-effects were observed in 2 patients. The authors consider that the results of this preliminary trial are encouraging; a further investigation in a larger series of patients is contemplated. *O. D. Standen*

Tuberculosis

36. **The Syndrome of Eventration of the Diaphragm as a Sequel of Tuberculosis in Childhood, with Reference to Six New Cases.** (Le syndrome d'éventration diaphragmatique, séquelle de l'invasion tuberculeuse chez l'enfant. À propos de six cas nouveaux)
J. RICHARD, V. CHEVALIER, and R. CAPELLE. *Archives françaises de pédiatrie* [*Arch. franç. Pédiat.*] **15**, 1042–1067, 1958. 10 figs., 33 refs.

Since 1951 the authors, working at the Policlinic, Tournai, Belgium, have seen 6 children who developed an eventration of one or other hemidiaphragm (in 5 on the left side) in association with a primary tuberculous infection of the lung on the same side. Paradoxical movement of the diaphragm or its immobility was demonstrated on screening. In all 6 cases the radiographic appearance of the diaphragm was known to have been normal before the tuberculous infection or during its early course.

In these and in similar reported cases the radiological appearances were striking, but the condition rarely produced symptoms and was usually discovered on routine x-ray examination. In the authors' cases the eventration remained permanent in spite of antibiotic treatment of the tuberculous infection, but other authors have reported occasional recovery of function after variable intervals. The cause of the paradoxical movement is considered to be a direct involvement of the phrenic nerve in caseous lymph nodes in the mediastinum, with resulting neuritis. The different anatomical course of the two phrenic nerves explains the greater frequency of left-sided involvement. The incidence of eventration in primary tuberculosis is low—in one reported series only 2 cases were found among 3,900 tuberculous children. Details of 31 cases previously reported in the literature are summarized in a table.
John Lorber

37. **Preventive Chemotherapy of Tuberculosis with Isoniazid.** (Quimioterapia preventiva da tuberculose pela isoniazida)
S. NEVES and N. ESPÍNDULA. *Revista brasileira de tuberculose* [*Rev. bras. Tuberc.*] **26**, 7–30, Nov., 1958. 8 figs., 36 refs.

After a rapid survey of the results reported from various countries regarding the treatment with isoniazid of contacts of patients with tuberculosis, the authors describe their own experience in treating 2,424 such contacts who completed the prescribed course of preventive therapy (namely, 10 mg. of isoniazid per kg. body weight daily over a period of 12 weeks) in the province of Espirito Santo, Brazil. Among the 50% of these subjects followed up for at least one year there were no deaths, and in only 5 cases was there any pulmonary tuberculous infection. Intolerance to the drug was negligible. Of those who did not complete the course, lack of interest, usually by the subject's father, accounted for about half the cases, while in most of the others contact was lost simply because of the nomadic tendencies of the inhabitants of this province. *Paul B. Woolley*

38. **A Clinical Study of the Haemagglutination Reaction in Tuberculosis.** [Monograph, in English]
J. SPÅNGBERG. *Acta tuberculosea Scandinavica* [*Acta tuberc. scand.*] Suppl. 46, 1–96, 1959. Bibliography.

39. **The Treatment of Tuberculosis of the Skin with Vitamin C.** (Zur Behandlung der Hauttuberkulose mit Vitamin C)
W. GERTLER, H. GARTMANN, H. GOLLA, A. KNAPP, and H. SIELER. *Zeitschrift für Tuberkulose* [*Z. Tuberk.*] **112**, 149–160, 1958. Bibliography.

At the Skin Clinic of the Karl Marx University, Leipzig, 13 patients with tuberculosis of the skin were given daily intravenous injections of 2 g. of L-ascorbic acid for 3 months together with standard treatment with either vitamin D_2 or anti-tuberculous drugs. The addition of ascorbic acid produced euphoria and increase of appetite, but had no appreciable effect on the response of the tuberculous lesion to treatment. This lack of direct effect *in vivo* was confirmed by experiments on guinea-pigs. *In vitro*, however, the growth of tubercle bacilli on Holin's egg medium was partly inhibited by ascorbic acid in a concentration of " 100 mg.% " [? 100 mg. per 100 g. medium] and completely inhibited by " 500 mg.% ", but was actually enhanced by concentrations of less than " 100 mg.% ". *P. Mestitz*

RESPIRATORY TUBERCULOSIS

40. **The Rapid Treatment of Pulmonary Tuberculosis.** (Le traitement rapide de la tuberculose pulmonaire)
J. L. GOMEZ PIMIENTA. *Acta tuberculosea Belgica* [*Acta tuberc. belg.*] **49**, 604–619, Oct., 1958 [received Jan., 1959]. 15 refs.

The author considers that in most cases pulmonary tuberculosis can be regarded as a " localized anatomopathological problem " and not as an ordinary infective illness. The lesion is of an irreversible character, requiring collapse or extirpation therapy, and as the infective element is not important this treatment should be carried out at the earliest possible moment. In support of this thesis he quotes the results obtained in several groups of cases selected from amongst those treated at the Instituto Nacional de Neumologia, Mexico. [The method of selection is not specified.] Thus of 50 patients who have been followed up for more than 10 years since treatment by collapse therapy, all are well and working, although the average period of stay in hospital was only 10 days for moderate cases and 46 days for advanced

cases and the average period off work 75 days and 110 days respectively. In another group of 266 patients who were treated by early thoracoplasty or resection and returned to manual work immediately after discharge there were 5 cases of relapse over a period of 5 years. Among 88 cases in which thoracoplasty was carried out in the active phase of the disease there was one operative death. There were no operative complications in the survivors, and among the 83 patients who were regarded as cured on leaving hospital there were no relapses. Among 132 cases in which resection was performed there were 4 operative deaths. Bronchopleural fistula was a complication in 9 cases. Of the 119 patients who were discharged cured, 2 relapsed. *G. M. Little*

41. **Observations on the Administration of Kanamycin to Patients with Tuberculosis**
K. W. WRIGHT, A. D. RENZETTI, J. LUNN, and P. A. BUNN. *American Review of Tuberculosis and Pulmonary Diseases* [*Amer. Rev. Tuberc.*] **79**, 72–77, Jan., 1959. 2 figs., 6 refs.

In this paper are described the effects of kanamycin treatment of 12 patients with chronic cavitary pulmonary tuberculosis, 11 of whom had tubercle bacilli resistant to streptomycin, isoniazid, and PAS; photochromogenic acid-fast bacilli were present in the sputum of the remaining patient. During the period of treatment, which extended up to 6 months, blood concentrations above the usual inhibitory levels were achieved with a daily dose of 0·5 g. kanamycin administered intramuscularly, and were maintained for 8 hours. Two patients who were initially treated with 1 g. of kanamycin daily lost their hearing. Granular casts appeared in the urine of all patients. No serious toxic effects were noted in the vestibular apparatus or in the renal, hepatic, and haematopoietic systems. Eosinophilia was common, but no other sensitivity phenomena of significance were observed. Half the patients developed bacterial resistance at 60 days and all the patients at 120 days.

Clinical and radiological evaluation indicated that kanamycin had sufficient antituberculous activity in man to warrant a trial in combination with another antibacterial agent in a larger series of patients. Of additional interest was the observation that kanamycin inhibited the growth of a strain of photochromogenic acid-fast bacilli. This finding suggests that the drug should also be given further trial in the treatment of infections associated with atypical acid-fast bacilli.
A. J. Karlish

42. **Pulmonary Resection for Tuberculosis under Protection of Viomycin, Promizole and Pyrazinamide**
W. R. WEBB and K. SPARKUHL. *Diseases of the Chest* [*Dis. Chest*] **34**, 484–495, Nov., 1958. 2 figs., 23 refs.

The authors stress the difficulties which arise in the surgical treatment of patients suffering from pulmonary tuberculosis in whom the tubercle bacilli have become resistant to the usual chemotherapeutic drugs. They review the literature on this subject and comment on the high morbidity rate and high incidence of major complications in such cases, bronchopleural fistulae being particularly common after segmental resection. In an attempt to lessen these risks the authors, working at the Mississippi State Sanatorium, Jackson, have used viomycin in combination with either pyrazinamide or "promizole" (thiazosulphone) as a cover for pulmonary operations in 32 patients in all of whom the sputum was positive at the time of operation, the causative organism having proved resistant to the usual antituberculous drugs. All but 2 of these patients had received chemotherapy for more than one year, the majority for more than 18 months. In 28 cases the disease was far advanced, and therefore in only 3 was the operation confined to segmental resection, in the remainder being more extensive. The patients were given viomycin and one of the other two drugs for 2 weeks before operation and for 3 months after it; only one patient developed a toxic reaction to the drugs.

There were 4 surgical deaths in the series, but in only 2 of the remaining 28 cases was the disease deemed to be still active, the sputum in all the others becoming and remaining negative for up to 3 years after resection. The authors are convinced that viomycin in combination with one or other of the drugs mentioned has a place in prophylaxis against complications in drug-resistant cases of tuberculosis requiring surgical intervention.
J. R. Belcher

43. **Treatment of Tuberculous Pleural Effusions with Particular Reference to Adrenal Corticosteroids**
M. H. D. SMITH and N. MATSANIOTIS. *Pediatrics* [*Pediatrics*] **22**, 1074–1087, Dec., 1958. 4 figs., 36 refs.

It is pointed out that tuberculous pleural effusions are far from benign, especially when they occur in children, and that there are two essential factors in the successful management of cases—namely, active treatment with antimicrobial drugs to prevent extension of tuberculous disease and the prevention of pleural thickening and consequent impairment of ventilation. The quicker a pleural effusion absorbs, the less chance is there of fibrothorax. Corticosteroids inhibit fibroblastic activity and inflammatory responses to tuberculin.

The authors describe the management and treatment of 6 cases of tuberculous pleurisy in children aged 4 to 11 years seen at the New York University–Bellevue Medical Center. The diagnosis was based on the results of tuberculin tests, culture of gastric washings and pleural fluid, and pleural biopsy. Isoniazid in a dosage of 20 mg. per kg. body weight daily and *p*-aminosalicylic acid (PAS) in a dosage of 0·5 mg. per kg. body weight daily were given to 5 of the patients; the remaining patient received a similar dosage of isoniazid with streptomycin instead of PAS. Prednisone in a dosage of 1 mg. per kg. body weight daily was given with these drugs for 4 to 6 weeks and then gradually withdrawn over a period of 14 days. The patients were kept in bed only so long as they remained febrile.

There was rapid clinical improvement in 5 cases. Radiographs showed that large pleural effusions resolved in 2 to 14 days. No untoward effects of this treatment were observed and the authors conclude that it is both advantageous and safe. *Raymond Parkes*

Venereal Diseases

44. **Results of the Treatment of Gonorrhoea in the Birmingham Clinic**
G. KNIGHT. *British Journal of Venereal Diseases* [*Brit. J. vener. Dis.*] **34**, 223–226, Dec., 1958. 7 figs.

The results obtained at the Birmingham Clinic in the treatment of gonorrhoea in males during the years 1955, 1956, and 1957 are analysed. In the area served by the clinic there is a large immigrant population, mainly from the Caribbean but with a sprinkling of Indians and Pakistanis. The incidence of gonorrhoea increased over the 3-year period, and while the West Indians may have been initially responsible for the rise, it is clear from the figures given that the incidence increased in all racial groups, including white subjects.

Treatment consisted in one injection of 300,000 units of procaine penicillin as soon as the diagnosis was established and 0·5 g. of sulphathiazole 4 times a day for one week. Films and cultures after prostatic massage were taken once a week for one month after treatment and thereafter at monthly intervals for 6 months. The proportion of patients (16%) who defaulted after treatment and before any tests had been carried out remained constant in the years under review. No attempt was made to distinguish a relapse from a reinfection, all such cases being classified as failures. There was a marked increase in the number of failures in 1957 after a fall in 1956, especially in white patients. In the discussion the author states that the rise in the failure rate occurred rather later in the Birmingham area than in other areas, possibly because of the sulphonamide therapy, and that the tendency of the West Indian to become reinfected is diminishing. Gonorrhoea is still increasing in Birmingham, probably because of the difficulty of tracing the carrier contacts. *Leslie Watt*

45. **The Use of Pathogenic *Treponema pallidum* as Antigen in Complement-fixation Reactions.** (Utilisation de *Treponema pallidum* pathogène en tant qu'antigène pour réaction de fixation du complément)
A. VAISMAN, A. HAMELIN, and R. PRUDHOMME. *Annales de dermatologie et de syphiligraphie* [*Ann. Derm. Syph. (Paris)*] **85**, 642–649, Nov.–Dec., 1958. 28 refs.

Treponemes harvested from the testes of rabbits infected with the virulent Nichols strain of *Treponema pallidum* were washed free from testicular juice, suspended in 0·3% phenol-saline, and disintegrated by exposure to ultrasonic waves (960 kHz) for 30 minutes in an atmosphere of hydrogen to avoid oxidation. The resulting suspension of very fine particles was used at its optimum titre as the antigen in complement-fixation tests by the fifth-volume Kolmer technique. An antigen was prepared from the cultivable Reiter treponeme by a similar method.

Tests on 2,216 sera were carried out with both these antigens at the Institut Alfred-Fournier, Paris, in parallel with the treponemal immobilization (T.P.I.) test and 4 standard tests for syphilis (S.T.S.) with lipoidal antigens (the Kolmer and Demanche complement-fixation tests and the Kline and Kahn tests). The sera were selected in that they included a majority which had shown discrepancies between the results of the T.P.I. test and the S.T.S. The results of the T.P.I. test were used as a baseline for the estimation of the sensitivity and specificity of the various other tests, the group of S.T.S. being considered as a whole.

A positive T.P.I. reaction was obtained with 1,666 sera. Of these, 94·6% gave a positive complement-fixation reaction with the antigen made from virulent *T. pallidum* and 88·4% with that from the Reiter organism, while only 61·8% gave a positive result with the S.T.S. The remaining 550 sera gave negative T.P.I. reactions; 24 of these gave positive reactions with the Nichols-strain antigen, 38 with the Reiter antigen, and 77 with the S.T.S. [No clinical information is given about those patients whose sera gave discrepant results.] The authors conclude that the antigen made from the virulent organism is preferable to that made from the Reiter strain because of its greater sensitivity and specificity. *A. E. Wilkinson*

46. **Epidemiological Study of Infectious Syphilis**
J. A. SOQUEL, W. O. HOSKING, C. H. MONTGOMERY, and F. K. LAURENTZ. *Southern Medical Journal* [*Sth. med. J. (Bgham, Ala.)*] **52**, 199–203, Feb., 1959. 1 fig., 3 refs.

47. **Donovanosis of the Anus in the Male: an Epidemiological Consideration**
M. MARMELL. *British Journal of Venereal Diseases* [*Brit. J. vener. Dis.*] **34**, 213–218, Dec., 1958. 8 figs., 19 refs.

In this paper from the Harlem Hospital, New York City, the author reports 10 cases of donovanosis (granuloma inguinale) in which the lesions affected the anus without involvement of the genitalia. The patients were males (7 coloured, 2 Puerto Ricans, and 1 white), and all except the white subject admitted to being passive homosexuals. The diagnosis was established by the demonstration of *Donovania granulomatis* in tissue smears stained with Wright's or Giemsa stain. A review of the literature showed that 44 out of a series of 48 patients with anal donovanosis admitted to passive pederasty. The marked association between anal donovanosis in the male and admitted homosexuality appears to suggest a causal relationship between the two; venereal transmission is considered to be more plausible than some of the other suggested methods of transmission.

Certain features of donovanosis still require elucidation —namely, the variable incubation period and the fact that symptoms rarely appear in coital partners of patients with this disease. *Leslie Watt*

Tropical Medicine

48. **Clinical Trials with Bephenium Hydroxynaphthoate against Hookworm in Ceylon**
L. G. GOODWIN, L. G. JAYEWARDENE, and O. D. STANDEN. *British Medical Journal* [*Brit. med. J.*] **2**, 1572–1576, Dec. 27, 1958. 2 figs., 9 refs.

Several salts of bephenium (benzyldimethyl-2-phenoxyethylammonium), the parent substance of a new series of quaternary ammonium compounds, were tested for effectiveness against hookworm infections (*Necator americanus*) in 284 patients under hospital and field conditions in Ceylon. Bephenium hydroxynaphthoate was selected as the most suitable salt, this substance being readily acceptable and its lack of toxicity enabling a standard dose to be administered irrespective of age and the gravity of the clinical picture.

A single dose of 2 to 3 g. of the base was as effective as a standard dose of tetrachlorethylene, and patients too ill to receive the latter tolerated bephenium hydroxynaphthoate without any sign of toxic effects. Treatment with multiple doses of the same magnitude, given either 2 to 3 times daily or on successive days, was of advantage in the presence of diarrhoea, particularly in children. No purge is required after the administration of bephenium hydroxynaphthoate, and the drug is also effective against concurrent roundworm infection. The detailed results are tabulated. *Max Mayer*

49. **Influence of Maternal Malaria on Newborn Infants**
H. M. ARCHIBALD. *British Medical Journal* [*Brit. med. J.*] **2**, 1512–1514, Dec. 20, 1958. 7 refs.

The author has investigated the effect produced by malarial infection of the placenta on the birth weight of the baby on the basis of data collected from a number of centres, mostly medical institutions, in Northern Nigeria.

The observations were made on 440 infants born alive in single deliveries after full-term pregnancies. Of these, 62 were born from malarious placentae (*Plasmodium falciparum*), and of this number 13 (20·6%) weighed 5½ lb. (2,495 g.) or less as contrasted with 31 (8·2%) born from uninfected placentae. The mean weight of the infected group was 6 lb. 2 oz. (2,778 g.) with a standard deviation of 14·4 oz. (408 g.) compared with 6 lb. 12½ oz. (3,706 g.) with a standard deviation of 16·4 oz. (465 g.). Examination of the figures with respect to the race to which the mother belonged showed that infants of infected mothers of the indigenous races were, on the average, of lower birth weight than those of mothers from the Southern Region. This is consistent with the hypothesis that immunity is less well established in the people of Northern Nigeria than in the people bred farther south where malaria is stable. Further evidence for this is shown by the high proportion of mothers with infection both in the blood and in the placenta (79%) as compared with the proportions found among mothers in more endemic areas—for example, 43% in a Lagos group. Such coincident infection probably indicates that "the woman has not succeeded in mastering the infection" and is consistent with earlier impressions that immunity to malaria in Northern Nigeria is not firmly established. *I. M. Rollo*

50. **Chloroquine per Rectum for Malaria in Children**
L. J. BRUCE-CHWATT and F. D. GIBSON. *British Medical Journal* [*Brit. med. J.*] **1**, 894–896, April 4, 1959. 15 refs.

A comparative trial of oral and rectal administration of chloroquine for the treatment of malaria was carried out on 28 children admitted to the Royal Orthopaedic Hospital, Igbobi, Lagos, Nigeria, and found to be suffering from malaria. A first group of 10 patients were given chloroquine sulphate by mouth in a single dose containing 300 mg. of chloroquine base. Another similar group of 12 children were given a single chloroquine sulphate suppository containing 300 mg. of base, while the remaining 6 children were given one suppository daily for 5 days, thus receiving a total dose of 1,500 mg. of chloroquine base. All the children were infected with *Plasmodium falciparum*, while in 14% *P. malariae* was also present in the blood.

A single dose of 300 mg. given per rectum cleared the blood of *P. falciparum* schizonts in only 38% [*sic*] of cases compared with 100% when the same dose was given by mouth. When 5 daily doses were given per rectum clearance was complete but slow, the average clearance time being 3 days as against 1·8 days with oral therapy. Excretion of chloroquine in the urine after oral administration of the drug averaged 20% of the total dose, whereas after rectal administration it was only 5%.

It is concluded that the rectal administration of chloroquine (which is widely practised in French overseas territories) cannot replace the oral method when speed of action is of importance, although it may be of use in special circumstances, particularly in paediatric practice. *R. R. Willcox*

51. **Protein-calorie Malnutrition in Tropical Preschool Children. (A Review of Recent Knowledge.)** [Review Article]
D. B. JELLIFFE. *Journal of Pediatrics* [*J. Pediat.*] **54**, 227–256, Feb., 1959. 7 figs., bibliography.

52. **Increased Amino-aciduria in Infants with Kwashiorkor Fed Natural and Synthetic Diets**
H. E. SCHENDEL, A. ANTONIS, and J. D. L. HANSEN. *Pediatrics* [*Pediatrics*] **23**, 662–675, April, 1959. 24 refs.

Nutrition and Metabolism

53. **Lowering Blood Lipid Levels by Changing Food Patterns**
H. B. BROWN and I. H. PAGE. *Journal of the American Medical Association* [*J. Amer. med. Ass.*] **168**, 1989–1995, Dec. 13, 1958. 5 figs., 17 refs.

There is increasing circumstantial evidence that a high blood cholesterol level may be related causally to the occurrence of atherosclerosis. Since the blood cholesterol level is in part dependent on the amount and quality of fat in the diet, a reduction in the incidence and severity of atherosclerosis may depend similarly on the adoption of new food patterns.

Two different types of diet can be used for reducing the serum cholesterol level. The first is the low-fat diet, in which only 10% to 15% of the total calories are provided in the form of fat, and which is at the same time basically a reducing diet. It should not contain more than 30 g. of fat daily, most of which should be given at the same time, thus providing at least one satisfying meal a day and securing a more complete catabolism of the fat.

The second type, the vegetable-oil diet, is basically similar to the low-fat diet in that its content of animal fats (such as butter, margarine, lard, egg-yolk, and pork and other fatty meat) is reduced, but the total fat content is augmented by the addition of certain vegetable oils. Thus the vegetable-oil diet used at the Cleveland Clinic, Ohio, providing 2,000 Calories daily, consists of 225 g. of carbohydrate, 70 g. of protein, and 90 g. of fat (meat providing 15 g. and vegetable oil 75 g.). A modified vegetable oil which consists of 94% cottonseed oil and 6% stearin additives is used; this can easily be emulsified and made into a spread for use on bread or reconstituted with fat-free milk solids into "milk", "cream", or "ice-cream", thus enabling the diet to be adopted for the whole family and making it less monotonous.

During a trial of this diet lasting 21 days in 4 active young subjects the serum cholesterol level was reduced by 40 to 80 mg. per 100 ml. in all cases. The same diet has been given for many months to 16 patients with hypercholesterolaemia, the group including cases of atherosclerosis with angina pectoris or myocardial infarction, xanthomatosis, diabetes, familial hypercholesterolaemia, and hypertension. Most of these patients had previously been taking a low-fat diet, which had successfully reduced the serum cholesterol level, but in many cases a further fall was achieved with the vegetable-oil diet.

[Similar diets have been in use in London since 1956 with most satisfactory results. With skilful use of some of the unsaturated vegetable oils they can be made sufficiently palatable and very similar in taste to the usual Western diet. The use of these experimental diets is justified in appropriate cases, but little is yet known about the effects of their long-term use and the time has not come to advocate a complete change in our dietary pattern. It should be noted that although the ingestion of fats containing a high proportion of unsaturated fatty acids markedly reduces the serum cholesterol level, it does not modify in the same way the many other lipids in the blood which may also be concerned in atherogenesis.] *Z. A. Leitner*

54. **Limitation of Radioiodine as a Label for Fat**
E. VAN HANDEL and D. B. ZILVERSMIT. *Journal of Laboratory and Clinical Medicine* [*J. Lab. clin. Med.*] **52**, 831–839, Dec., 1958. 11 refs.

Chemical procedures for the determination of I^{131} lipid fractions in whole blood, plasma, and tissues are discussed. I^{131} labeled triolein, administered intravenously as an emulsion, disappears at the same rate as natural fats. After oral administration of I^{131} triolein the concentration of I^{131} triglyceride in dog plasma during the period of alimentary lipemia is lower than that of the chemically determined fat. This difference between the specific activity of fed fat and plasma fat already exists in lymph, as shown by the low specific activity of dog and rat lymph compared to that of the administered fat. Comparison of I^{131} and C^{14} triolein showed that dilution by an endogenous triglyceride pool cannot account for the observed decrease in specific activity. The distribution of orally administered C^{14} oleic acid and C^{14} stearic acid in the neutral fat fraction of carcass is fairly similar to that of I^{131} oleic acid. However, in liver, where rapid incorporation of C^{14}-labeled fatty acids into phospholipid fractions occurs, I^{131} oleic acid was found to be absent and thus gives an erroneous picture of the distribution of dietary fatty acids.—[Authors' summary.]

METABOLIC DISORDERS

55. **Etiology of Severe Obesity: A Study of Five Cases**
M. B. FERTMAN. *Journal of the American Geriatrics Society* [*J. Amer. Geriat. Soc.*] 7, 38–50, Jan., 1959. Bibliography.

The multiplicity and variety of the factors concerned in the aetiology of obesity are discussed in this paper from the Stanford University School of Medicine, San Francisco. It is emphasized that, at least in relation to excessive caloric intake, which is a well-established factor, the central nervous system is involved. This may be a result of organic disease, trauma, or a "functional" state, as in habit patterns and neuroses. Metabolic factors may be involved either primarily or secondarily, and any or all of these mechanisms may be triggered or altered by heredity, toxic agents, stress, pregnancy, or specific pathological conditions.

A study is reported of 5 extremely obese females whose maximum weight was 274 to 403 lb. (124·7 to 182·3 kg.). In 4 there was a family history of obesity. An excessive appetite was admitted by 4, who also complained of nervousness or a nervous disorder. One of these had suffered from encephalitis, while in another there had been sudden precipitous gains in weight in association with attacks of severe infectious disease. In 3 cases prolonged rest in bed may have been a causative or contributory factor. Gonadal changes, either physiological or pathological, were associated with weight gain in 4 of the 5 patients. The author states that one case differed markedly from the others, special features being: sudden onset of obesity, advanced hypertension, "asserted absence of hyperphagia or over-eating and mental distress", and the absence of known obesity in the family.

It is suggested that the careful study of the endocrine glands and hypothalamus at necropsy on patients with severe obesity would be of the utmost value in understanding the development of this condition.

A. G. Mullins

56. **Periodic Paralysis. Sodium Metabolism and Aldosterone Output in Two Cases**
R. V. Jones, R. R. McSwiney, and R. V. Brooks. *Lancet* [*Lancet*] **1**, 177–181, Jan. 24, 1959. 3 figs., 21 refs.

Previous workers have suggested that in periodic paralysis potassium enters the muscle cells during the paralytic period. In many cases the entry of glucose into these cells appears to have caused the potassium shift. Conn *et al.* (*Lancet*, 1957, **1**, 802; *Abstr. Wld Med.*, 1957, **22**, 185) concluded that the shift of potassium during the paralysis was necessarily preceded by a rise in intracellular sodium.

In this investigation carried out at St. Thomas's Hospital, London, on 2 patients with periodic paralysis associated with hypokalaemia the metabolism of sodium and potassium and the urinary aldosterone excretion were studied for 24 hours during the induction of an episode of paralysis with glucose and insulin. Full case reports are given. In one patient there was a twofold increase in urinary aldosterone excretion between 10 a.m. and noon during the process of induction, but the total 24-hour excretion was not altered. In the second patient the urinary aldosterone excretion was low and showed no increase in the 24 hours during which the paralysis was developing. The potassium balance in the first patient was negative both at the onset of paralysis and in the developed state, but in the other it was positive. Cases are reported in the literature of potassium retention, but also of negative potassium balance. The electroencephalographic (EEG) findings were abnormal in the first case and did not alter, whereas in the second case they were normal until paralysis set in, and then became abnormal. Other authors have reported normal EEG records both before and during paralysis.

Conn *et al.* (loc. cit.) had concluded that "retention of sodium is the primary factor which sets in motion the characteristic chain of events in an episode of periodic paralysis". The present authors, however, suggest that this is by no means invariable and not essential for paralysis. The observations in the 2 cases described suggest no over-all shift of sodium into or out of cells during the development of paralysis. As these patients did not give permission for muscle biopsy to be performed the possibility of shifts from bone and from one type of cell to another could not be excluded. From their findings the authors conclude that "sodium retention and increased excretion of aldosterone do not necessarily precede attacks of periodic paralysis in all cases" of this disorder.

M. R. Medhurst

57. **Diagnostic Considerations in Hypercalcemia: with a Discussion of the Various Means by Which Such a State May Develop.** [Review Article]
W. C. Thomas, T. B. Connor, and H. G. Morgan. *New England Journal of Medicine* [*New Engl. J. Med.*] **260**, 591–596, March 19, 1959. 2 figs., bibliography.

58. **The Xylose Tolerance Test as a Measure of the Intestinal Absorption of Carbohydrate in Sprue**
J. M. Finlay and K. J. R. Wightman. *Annals of Internal Medicine* [*Ann. intern. Med.*] **49**, 1332–1347, Dec., 1958. 1 fig., 38 refs.

The authors, at the Toronto General Hospital, have studied the value of a xylose tolerance test as a measure of intestinal absorption of carbohydrate for use in the diagnosis of the steatorrhoeas. Xylose, which is water-soluble, is not normally found in blood or urine, is not metabolized by the liver, and is phosphorylated during absorption. For the test 25 g. of xylose is given and blood levels estimated every hour for 5 hours, during which time the output in the urine is also measured.

The response to xylose was reproducible and not influenced by cortisone in healthy subjects. In patients with diseases other than gastro-intestinal higher blood levels and lower excretion rates were obtained, this effect being thought to be due either to age or to the effect of illness. The curves of patients with diarrhoea but without steatorrhoea were variable, but the majority showed unexpectedly increased levels. In cases of steatorrhoea flat curves with low renal excretion were obtained on 14 out of 16 occasions.

A good clinical response was obtained following treatment with cortisone in 6 out of 7 cases; in 5 of these the xylose absorption curve returned to normal. On a gluten-free diet, which had a good clinical effect in all of 6 cases, the response to xylose improved in 4 out of 5 cases, while in the sixth the response was normal initially and remained so during treatment. In secondary steatorrhoea (15 cases tested) no such abnormality was observed, the curve being normal in 9, flat in 4, and high in 2. After cortisone therapy one high curve returned to normal; the others were essentially unchanged.

The authors conclude that the test may well be of value in the diagnosis of the idiopathic from the secondary type of steatorrhoea and from other forms of diarrhoea, and that it may also be of value in the assessment of therapy in idiopathic steatorrhoea.

A. Gordon Beckett

Gastroenterology

59. **Secretion of Blood Group Antigens and Peptic Ulcer**
C. A. CLARKE, D. A. P. EVANS, R. B. MCCONNELL, and P. M. SHEPPARD. *British Medical Journal* [*Brit. med. J.*] **1**, 603–607, March 7, 1959. 13 refs.

The authors [who have been in the forefront of research into the connexion between blood-group substances and peptic ulceration] report from the University of Liverpool their latest studies of secretor status. Comparing the secretor status in controls (851) and patients with duodenal (1,104) and gastric (138) ulcers, they found a significant difference between duodenal and gastric ulceration with respect to the frequencies of ABH non-secretion (36·6% in duodenal and 27·5% in gastric ulcer; controls 24·3%). The liability to duodenal ulcer of different blood-group and secretor phenotypes was assessed on the basis of the findings in 521 consecutive cases of duodenal ulcer and 680 random controls. Group-O non-secretors were found to be 2½ times more liable to ulceration than secretors of Groups A, B, and AB. This is more than would be expected from the Group-O factor acting with the non-secretion factor, but the excess is not statistically significant. The differences between the phenotypes of patients with duodenal ulcer and of the general population are clear-cut, and one might expect to find similar differences between affected and unaffected sibs. However, the authors find that the phenotypes of unaffected sibs are almost identical with those of their affected relatives. They consider a susceptible racial strain (stratification) to be an unlikely explanation.

The authors have estimated the fucose content of the saliva of controls and of sibs with and without duodenal ulcer. They find this to be a good index of the total amount of blood-group substances if the ABO grouping and secretor status are known. Non-secretors of ABH are presumed to secrete Lewis substance only. Evidence is produced suggesting that there is no difference in the total amount of blood-group substances as between patients with duodenal ulcer and controls.

The authors conclude that the mechanism of the association between blood-group substances and duodenal ulcer must be an immunological one due to the different antigenic properties of the different groups.

[This paper should be read in full, since the wealth of material precludes adequate summarization.]

B. F. Swynnerton

60. **Excess Blood-group Substance A in Serum of Patient Dying with Carcinoma of Stomach**
M. BARBER and I. DUNSFORD. *British Medical Journal* [*Brit. med. J.*] **1**, 607–609, March 7, 1959. 9 refs.

A case is reported from the National Blood Transfusion Service, Sheffield, in which difficulty was encountered in determining the blood group of a woman admitted to hospital in the terminal stage of carcinoma of the gastric cardia with metastases. Further investigation revealed the presence of excessive amounts of A substance in her serum, which neutralized the anti-A antibodies before they could agglutinate her erythrocytes. Excessive amounts of H substance were also found in the serum. Her secretor status was not determined, but as her Lewis type was Le(a−b+) it was assumed that she was a secretor of A and H. In a series of 500 Group-A sera from blood-donor samples only one person was found to have comparable levels of A substances. In 12 other cases of gastric carcinoma no excess of group-specific substances was discovered.

The association between carcinoma of the stomach and Group-A blood is now well established. The findings in the case here reported may be fortuitous, but it is possible that the large amounts of A substances produced the cancer or were produced by it. The authors suggest that further work along the lines they describe is indicated in patients with gastric carcinoma.

B. F. Swynnerton

61. **Duodenal Irrigation with a Weak Solution of Procaine in Cases of Dyskinesia of the Biliary Tract and of Cholecystitis.** (Внутридуоденальные новокаиновые орошения при дискинезиях желчевыводящих путей и холециститах)
N. I. IONOVA. *Клиническая Медицина* [*Klin. Med.*] **37**, 91–96, Feb., 1959. 2 figs., 21 refs.

In 103 patients with biliary dyskinesia irrigation of the duodenum was carried out by means of a duodenal tube with 20 ml. of a 0·5% solution of procaine warmed to 37° C. Each patient received 5 to 6 irrigations at intervals of 1 to 2 days. It is reported that both in the hyper- and hypotonic and in the hyper- and hypokinetic forms of dyskinesia this treatment helped to restore the function of the gall-bladder to normal. It has also proved useful in cases of catarrhal cholecystitis in which functional disturbances of the biliary system were clinically prominent.

A. Orley

62. **Ammonia Intoxication Treated by Hemodialysis**
J. E. KILEY, J. C. PENDER, H. F. WELCH, and C. S. WELCH. *New England Journal of Medicine* [*New Engl. J. Med.*] **259**, 1156–1161, Dec. 11, 1958. 6 figs., 8 refs.

The authors discuss the application of haemodialysis to the treatment of hepatic coma and report their experience in 5 cases at the Albany Hospital, Albany, New York. All the patients had advanced liver disease with ascites and were in coma, with high blood ammonia levels, following intestinal bleeding. Although it was difficult to measure accurately the total amount of ammonia removed during dialysis, calculation from the change in blood ammonia content during passage through the artificial kidney and the rate of flow indicated that large quantities of ammonia were in fact removed. Two of the 3 patients in whom no biochemical abnormalities were found apart from ammonia intoxication came out of coma. In the 2 remaining patients other biochemical

abnormalities associated with uraemia and oliguria were present, but temporary improvement was noted, which was dramatic in one case. In each case bleeding was stopped by oesophageal tamponade before dialysis was started, and there was no renewal of bleeding as a result of heparinization.

Although no noteworthy clinical improvement occurred in any case until some time after the dialysis had been completed, the authors consider that the improvement eventually obtained was due at least in part to the treatment. Dialysis is likely to be of most value in hepatic coma precipitated by massive haemorrhage. However, as all 4 patients who were improved by dialysis subsequently died of renewed alimentary haemorrhage, treatment by this complex method is justifiable only if a portacaval anastomosis can be performed to prevent further bleeding. It is unlikely to be of value in cases of coma due to advanced liver-cell failure, but in cases of combined uraemia and ammonia intoxication dialysis may result in a striking improvement. *A. E. Read*

63. **Exudative Enteropathy. Abnormal Permeability of the Gastrointestinal Tract Demonstrable with Labelled Polyvinylpyrrolidone**
R. S. Gordon. *Lancet* [*Lancet*] **1**, 325–326, Feb. 14, 1959. 2 figs., 9 refs.

Cases have been reported by various authors in which a persistently low plasma protein level, associated with oedema, has been found together with an increased rate of turnover of plasma albumin, as measured with albumin labelled with radioactive iodine (^{131}I). This syndrome of "hypercatabolic hypoproteinaemia" has now been further investigated at the National Heart Institute, Bethesda, Maryland, by the intravenous injection of ^{131}I-labelled polyvinylpyrrolidone (PVP), a polymer used as a plasma protein substitute which, unlike labelled albumin, is not broken down in the alimentary tract should it gain entry to it, and can therefore be estimated in the faeces. It was found that in 41 normal subjects no more than 1·5% of the dose of ^{131}I–PVP was excreted in the faeces, whereas in 9 subjects with "hypercatabolic hypoproteinaemia" the faecal excretion of ^{131}I–PVP always exceeded this level and in one case reached 20%. There was an inverse relationship between the serum albumin level and the faecal output of ^{131}I–PVP. It is postulated that the abnormally rapid disappearance of albumin from the plasma is caused by excessive loss of protein into the alimentary tract in this condition, for which the name "exudative enteropathy" is suggested. *D. A. K. Black*

64. **Gastrointestinal Protein Loss in Idiopathic (Hypercatabolic) Hypoproteinaemia**
M. Schwartz and S. Jarnum. *Lancet* [*Lancet*] **1**, 327–330, Feb. 14, 1959. 7 figs., 42 refs.

In 1957 the authors (*Brit. med. J.*, **1**, 14) distinguished a type of hypoproteinaemia associated with rapid disappearance of labelled albumin from the blood which they described as "hypercatabolic hypoproteinaemia". They now report the investigation of 4 cases of this syndrome with ^{131}I-labelled polyvinylpyrrolidone (PVP) in the way described by Gordon [see Abstract 63] and confirm the excessive loss of ^{131}I–PVP into the alimentary tract. They also demonstrated an excessive loss of ^{131}I-albumin in the gastric juice of one patient, whose serum protein level returned nearly to normal after a subtotal gastrectomy, the stomach showing hypertrophic gastritis. In 2 other patients the abnormal loss of protein was into the small intestine, which was found on laparotomy to be oedematous, with enlarged lymph nodes in the mesentery; the process was too extensive to permit of resection. *D. A. K. Black*

65. **Cortisone and Corticotrophin in Ulcerative Colitis**
S. C. Truelove and L. J. Witts. *British Medical Journal* [*Brit. med. J.*] **1**, 387–394, Feb. 14, 1959. 17 refs.

A therapeutic trial of cortisone and corticotrophin in ulcerative colitis was carried out at centres in Britain by a limited number of physicians specially interested in this disease. The trial was divided into three parts designed respectively to determine whether: (1) cortisone and corticotrophin differ in efficacy in the acute attack of ulcerative colitis; (2) a small maintenance dose of cortisone by mouth would ensure continuous clinical remission; and (3) a patient who had once responded to steroid therapy would be particularly likely to respond again when in relapse.

In the first part of the investigation it was found that corticotrophin produced more remissions than did cortisone (60·7% compared with 38·8%), although the percentage unaffected by treatment and the mortality were virtually the same in the two groups. Patients given corticotrophin relapsed almost half as frequently again as did those given cortisone. Corticotrophin was superior to cortisone in the treatment of patients admitted in relapse, inducing a remission in 70·5% compared with 37·0% with cortisone; in this group of patients 15·9% of those given corticotrophin and 26% of those given cortisone were unchanged or worse. Complications of steroid therapy, which included hypercortisonism, peptic-ulcer complications, mental disturbance, and monilial infections, occurred more frequently with corticotrophin.

In the second part of the trial it was found that maintenance therapy with 50 mg. of cortisone daily did not prevent relapse; indeed patients receiving such maintenance therapy suffered from relapse somewhat more frequently than did controls, although the difference was not statistically significant.

In the third part it was demonstrated that the response to cortisone in patients in relapse was similar to the response in the original attack. These results were similar to those obtained previously by the authors (*Brit. med. J.*, 1954, **2**, 375 and 1955, **2**, 1041; *Abstr. Wld Med.*, 1955, **17**, 34 and 1956, **19**, 364), although the dosage used was double that given in the original trial.

The authors do not recommend administration of corticotrophin as the first line of treatment during an initial attack, preferring the newer steroids by mouth or hydrocortisone derivatives per rectum, but they suggest that it may be the best form of steroid therapy for the severely ill patient in relapse. *A. Gordon Beckett*

Cardiovascular System

66. **Post-partum Heart Disease**
A. B. BENCHIMOL, R. D. CARNEIRO, and P. SCHLESINGER. *British Heart Journal* [*Brit. Heart. J.*] **21**, 89–100, Jan., 1959. 8 figs., 44 refs.

For many years the occasional occurrence of congestive heart failure of obscure origin in the puerperal period has been recognized. The initial signs of decompensation usually develop late in pregnancy and improve after delivery, but often recur with greater severity later in the puerperium. Death may occur in failure, or follow systemic embolization, though most of the patients recover. The condition has been variously attributed to toxaemia, hypertension, and myocarditis, the added haemodynamic strains of delivery and the puerperium being regarded as precipitating factors. The authors describe a group of cases of this type, in none of which was there any known pre-existing heart disease, encountered at the Hospital dos Servidores do Estado and the Fifth Medical Clinic of the University of Brazil, Rio de Janeiro. They conclude from their study of these cases that there is no single cause of puerperal heart disease but that, with care, separate causative mechanisms can usually be identified.

Toxaemia of pregnancy seemed to be the underlying cause in 8 cases in the authors' series. The symptoms and signs were those of left ventricular failure, pulmonary congestion, and congestive failure in normal rhythm. There was considerable cardiac enlargement and T-wave inversion temporarily in left ventricular leads. All these patients recovered, some bearing children normally later on. In another 3 cases probably due to toxaemia the illness ran a longer course, with pulmonary and systemic embolism, and 2 of the patients died; in one of these extensive fibrosis in the left ventricular myocardium, with mural thrombi, was found at necropsy. Non-specific myocarditis was diagnosed in 2 patients who had fever, leucocytosis, and a raised erythrocyte sedimentation rate. They had gross congestive failure 2 weeks or more after delivery, with cardiac enlargement and transient T-wave inversion. Both ultimately recovered. Hypertensive heart disease due to chronic pyelonephritis was considered to be the cause of the congestive failure in 2 cases, the condition being aggravated by a recurrence of urinary infection. Specific myocarditis was the cause of 2 fatal cases of congestive heart failure, in one of which the condition was correctly diagnosed during life as being due to Chagas's disease, while in the other miliary tuberculosis was found at necropsy. *J. A. Cosh*

67. **The Anomalous Origin of the Left Coronary Artery from the Pulmonary Artery**
J. D. KEITH. *British Heart Journal* [*Brit. Heart J.*] **21**, 149–161, April, 1959. 10 figs., 27 refs.

68. **Constrictive Pericarditis**
T. M. D. GIMLETTE. *British Heart Journal* [*Brit. Heart J.*] **21**, 9–16, Jan., 1959. 1 fig., 10 refs.

The author describes the aetiology, symptoms, signs, and treatment in 62 cases of constrictive pericarditis admitted to St. Thomas's Hospital, London. A tuberculous aetiology was demonstrated in 17 cases; other causes included carcinomatous infiltration and pyogenic infection, while in 39 cases the cause was unknown. A point of interest was the frequency of rheumatoid arthritis (5 cases). Symptoms included orthopnoea, paroxysmal nocturnal dyspnoea, and oedema. Among the signs were a raised jugular venous pressure (with M- or W-shaped pulsation), an increased systemic venous pressure, oedema, hepatomegaly (with cirrhosis in 6 cases), and ascites; pulsus paradoxus and an early diastolic sound were also frequent. Radiological examination showed true cardiac enlargement in 22 cases and pericardial calcification in 27 cases. There appeared to be some correlation between cardiac enlargement and a poor prognosis. Electrocardiographic abnormalities included atrial fibrillation (22 cases), bifid P waves, low QRS voltage, and flat or inverted T waves. Cardiac catheterization carried out in 10 cases showed the characteristic diastolic dip, but there was no indication from the intracardiac pressure of obstruction to blood flow.

Pericardiectomy was performed on 42 patients, of whom 15 were cured, 17 showed little change, and 10 died. A preliminary course of streptomycin was given to 12 patients thought to have tuberculous pericarditis. Better results were obtained in cases of acute constrictive pericarditis than in the chronic cases, presumably owing to associated myocardial disease in the latter.

The author concludes that immediate pericardiectomy is indicated in acute constrictive pericarditis, and that medical treatment, often followed by surgery, is best in the chronic cases. *Gerald Sandler*

69. **Effects of Sublingual Nitroglycerin on Pulmonary Arterial Pressure in Patients with Left Ventricular Failure**
J. B. JOHNSON, A. FAIRLEY, and C. CARTER. *Annals of Internal Medicine* [*Ann. intern. Med.*] **50**, 34–42, Jan., 1959. 5 figs., 3 refs.

It has been reported that nitroglycerin effectively relieves the breathlessness and retrosternal distress associated with paroxysmal dyspnoea. In this paper from Freedmen's Hospital, Washington, D.C., the haemodynamic alterations produced by nitroglycerin in 13 patients with either left or both left and right heart failure are described. Of the 13 patients, 9 had hypertensive heart disease and one was suffering from arteriosclerotic heart disease with angina pectoris; in 3 patients the heart failure was of unknown aetiology. Standard

right heart catheterization procedures were used. Cardiac output was determined by the direct Fick method, the brachial arterial pressure was measured through an indwelling needle, and the pulmonary wedge pressure was determined by the method of Hellems and his associates. After control values for cardiac output and pressure had been obtained 0·6 mg. of nitroglycerin was given sublingually, cardiac output and pressure measurements being repeated at short intervals during the succeeding 30 minutes.

The mean pulmonary arterial pressure was elevated in all the patients during the control period, ranging from 20 to 72 mm. Hg. Following administration of nitroglycerin there was a prompt fall of about 28 mm. Hg in 10 cases. The brachial arterial pressure showed little change. In 4 cases in which the pulmonary wedge pressure was measured there was a significant fall. In 12 cases the total pulmonary resistance fell sharply during the first 15 minutes. There was no consistent alteration in cardiac output or significant rise in the heart rate. One patient had an attack of angina pectoris during the trial, accompanied by a sharp rise in pulmonary arterial pressure and resistance. After sublingual administration of nitroglycerin the pain rapidly disappeared and the pulmonary arterial pressure and resistance fell almost to normal. *G. Clayton*

CHRONIC VALVULAR DISEASE

70. Mitral Commissurotomy. Comparison of Clinical and Hemodynamic Results One to Three Years after Surgery

P. KEZDI and H. U. WESSEL. *American Journal of Cardiology* [*Amer. J. Cardiol.*] **3**, 45–53, Jan., 1959. 12 figs., 22 refs.

A series of 93 patients with mitral stenosis have been carefully studied at the Wesley Memorial Hospital (Northwestern University Medical School), Chicago, before mitral valvotomy and again one to 3 years after the operation. Right cardiac catheterization was performed in all cases and left cardiac catherization in some before operation. Catheterization (mostly right-sided) was repeated after operation in 33 cases.

The critical mitral valve area (calculated by means of the formula of Gorlin and Gorlin) in pure stenosis was found to be about 1·6 sq. cm. Most of the patients in whom the aperture was larger than this were in Grade I of the functional classification of the New York Heart Association, with low pulmonary capillary wedge or left atrial pressure, low pulmonary arterial pressure, and low pulmonary arteriolar resistance, whereas most of the patients in Grade III had a valve area of less than 1 sq. cm. Mitral valve area did not correlate well with pulmonary arteriolar resistance, but correlated directly with mitral valve resistance. Most patients in Grade III had a moderately or markedly raised pulmonary arterial pressure and a decreased cardiac output.

After valvotomy symptomatic improvement usually paralleled haemodynamic improvement so long as no regurgitation was produced. Of the 33 patients who underwent cardiac catheterization after valvotomy, 15 had a mitral valve area of more than 1·5 sq. cm. without regurgitation (Group A), 7 had no regurgitation but a valve area of less than 1·5 sq. cm. (Group B), and 11 had significant regurgitation but the valve area was not calculated (Group C). Patients in Group A had marked symptomatic improvement, and the mean pulmonary arterial and pulmonary capillary wedge pressures were decreased, though the changes in cardiac output and pulmonary resistance were more variable. Patients in Group B had not improved much in functional grade, and the pulmonary arterial and capillary wedge pressures and pulmonary resistance had risen in most of them. Patients in Group C showed no haemodynamic changes and little change in functional grade.

Inadequate opening of the valve accounted for poor improvement after valvotomy in some cases, while restenosis had occurred in 6% of the patients on whom catheterization was repeated. In some cases the authors considered that pre-existing myocardial damage hindered functional improvement in spite of adequate valvotomy. In their opinion the production of moderate regurgitation will not prevent improvement if the obstruction is relieved. *D. Emslie-Smith*

71. Some Clinical Notes on Patients with Mitral Valvular Disease Who Have Had Mitral Valvuloplasty

E. RISS and S. A. LEVINE. *American Heart Journal* [*Amer. Heart J.*] **56**, 814–830 and 831–845, Dec., 1958. 15 refs.

Patients who have had surgical treatment of mitral disease while under the care of the authors at the Peter Bent Brigham Hospital, Boston, Massachusetts, provide the basis for a comprehensive review of the criteria for selection for operation and the results of surgery in this type of rheumatic heart disease. The patients, numbering 72, were aged from 27 to 62 years, with an average in the 61 women of 40 years and in the 11 men of 47 years. There were 6 operative deaths and a further 5 deaths during the follow-up period, which averaged 3½ years.

Raised blood pressure was associated with somewhat less favourable results. Very loud apical systolic murmurs were noted in a few cases of " tight " mitral stenosis, though an absence of murmur was more usual, and the loudness of the diastolic murmur was no guide to the degree of stenosis. Calcification of the valve made the operation less safe and was associated with less satisfactory results. Attempts to restore normal rhythm in cases of established auricular fibrillation were not often successful, and the authors think it better not to attempt this. A history of peripheral embolism preoperatively increased the operative risk, but late embolic phenomena did not occur in this series. Electrocardiographic signs of right ventricular hypertrophy with an absence of those of left ventricular hypertrophy were among the criteria for the selection of cases, and only one case of combined right- and left-sided hypertrophy in which left-sided hypertrophy predominated was regarded as suitable for operation. While satisfactory results were obtainable in patients over 50 years of age, increasing years reduced the chances of a favourable result. The

best results occurred in the cases with the most severe stenosis.

The authors conclude that the patients with mitral valvular disease most likely to benefit from surgery are those who have pure stenosis and are appreciably disabled, with evidence of deterioration. *J. R. Sinton*

72. Acetylcholine and the Pulmonary Circulation in Mitral Valvular Disease

B. SÖDERHOLM and L. WERKÖ. *British Heart Journal* [*Brit. Heart J.*] **21**, 1–8, Jan., 1959. 2 figs., 5 refs.

The effect of acetylcholine injection into the pulmonary artery on the pressure in the pulmonary circulation was studied in 13 cases of mitral valvular disease at Sahlgrenska Sjukhuset, Göteborg, Sweden. The cardiac output was determined according to the direct Fick principle. Acetylcholine was infused into the pulmonary artery, the dose being increased until an effect on pulmonary arterial pressure was noted (3 to 14·5 mg. per minute); infusion was then continued at this dosage. The cardiac output was determined in each patient before and after acetylcholine infusion, first at rest and then after exercising at 100 kg. per minute.

Both at rest and with exercise there was a significant fall in arterial oxygen saturation and mean pulmonary arterial pressure after acetylcholine infusion. After exercise acetylcholine infusion also caused a significant increase in cardiac output, but this did not occur at rest. These changes were equally well produced when patients with an almost normal pulmonary arterial pressure at rest performed light exercise. In no case did acetylcholine infusion completely suppress the rise in pulmonary arterial pressure which occurred with exercise, the suggested reasons for this being an increased heart rate with decreased left ventricular filling time and pulmonary vascular constriction.

The authors have thus confirmed that acetylcholine can lower pulmonary arterial pressure and decrease pulmonary vascular resistance in some cases of mitral valvular disease, although they have been unable to determine whether this decrease is due to its effect on the mechanism which increases the pulmonary arterial pressure during the development of mitral valvular disease. The decrease in arterial oxygen saturation is a new finding, and the authors suggest that this is probably due to the action of acetylcholine in increasing intrapulmonary shunting of blood through poorly ventilated areas. *Gerald Sandler*

73. The Myocardial Factor in Mitral Valve Disease

H. A. FLEMING and P. WOOD. *British Heart Journal* [*Brit. Heart J.*] **21**, 117–122, Jan., 1959. 1 fig., 21 refs.

In a review of 750 cases of mitral stenosis treated at the Brompton and National Heart Hospitals, London, during the past 8 years a small group (24 cases; 3·2%) was found in which the valvular lesion was trivial and the symptoms were attributable primarily to myocardial disease. Usually this diagnosis could be made clinically and cardiac catheterization merely provided confirmation, but in some cases it was made only after full investigation. The symptoms were those of dyspnoea, oedema and fatigue, often of some years' duration and intermittent. There was auscultatory evidence of mitral stenosis, which was usually pure, though in 9 cases a pansystolic murmur was heard. No patient had a high pulmonary vascular resistance, pulmonary embolism, coronary disease, hypertension, or active carditis.

Comparison was made with a series of 150 patients chosen for mitral valvotomy which has previously been reviewed by Wood (*Brit. med. J.*, 1954, **1**, 1051; *Abstr. Wld Med.*, 1954, **16**, 213). The present group was rather older (average age 43 years against 37) and had a greater preponderance of women than the previous one; on the average the duration of symptoms was longer, but there did not appear to be a more serious past history of rheumatism. Atrial fibrillation was present in all cases in the present group compared with 41% of those in the surgical group, and probably for this reason systemic embolization was commoner (46% against 13%). There was no unusual degree of cardiac or left atrial enlargement and no specific changes in the electrocardiogram. Catheterization revealed a low cardiac output, no great increase in left atrial pressure at rest, and a normal or moderately increased pulmonary vascular resistance.

There was little direct evidence of myocardial disease in these patients and it seemed that the arrhythmia itself might play an important part in causing the symptoms and embolization. Sustained digitalization is valuable in this type of case, and prophylactic anticoagulant therapy may well be justified. *J. A. Cosh*

74. Cardiac Ventriculography in the Selection of Patients for Mitral Valve Surgery

J. F. URICCHIO, J. S. LEHMAN, W. M. LEMMON, R. A. BOYER, and W. LIKOFF. *American Journal of Cardiology* [*Amer. J. Cardiol.*] **3**, 22–27, Jan., 1959. 1 fig., 15 refs.

At the Hahnemann Hospital, Philadelphia, 42 patients with isolated mitral valvular disease were subjected to injection of a radio-opaque medium into the left ventricle by direct puncture through the thoracic and ventricular walls, rapid serial radiography being carried out during and after the injection. The amount of regurgitation was assessed from the intensity of opacification of the left atrium, with due regard to its size, and graded 1+ to 4+. At subsequent operation the degree of regurgitation as assessed by palpation was compared with the radiographic assessment. A significant degree (2+ or more) of opacification of the left atrium was seen in none of the 14 patients in whom pure mitral stenosis or only a minor degree of incompetence was found at operation, no opacification at all being noted in 9 of these. On the other hand in all the 28 patients with significant mitral incompetence on palpation the opacification was graded 2+ or more.

The authors claim that the technique is useful in assessing the degree of mitral incompetence in candidates for mitral commissurotomy, though it is not without risk, intramyocardial injection of the opaque medium being the chief hazard. They report that 2 deaths have occurred in the performance of more than 200 ventriculographies. *D. Emslie-Smith*

75. **Pulmonary Function in Mitral Valve Disease**
G. C. DOGLIOTTI, P. F. ANGELINO, A. BRUSCA, R. GARBAGNI, F. GAVOSTO, G. MAGRI, and E. MINETTO. *American Journal of Cardiology* [*Amer. J. Cardiol.*] **3**, 28–39, Jan., 1959. 2 figs., 36 refs.

Hemodynamic and ventilatory studies were carried out [at the Surgical Clinic of the University of Turin] in a large series of patients who underwent mitral surgery for mitral stenosis or insufficiency.

A diminution of cardiac index was found, which paralleled the narrowing of the mitral orifice. However, left ventricular failure seemed to be operative in some of the cases, even in the presence of pure, tight mitral stenosis. This hypothesis was also suggested by the observation that pulmonary artery and venous wedge pressures were significantly higher in patients with combined heart failure, independently of the size of the mitral orifice. A positive linear correlation was found between pulmonary artery pressures and pulmonary vascular resistances, when the latter were more than 200 and less than 900 dynes sec. cm^{-5}. No significant increase of pulmonary blood volume could be found in patients with mitral stenosis.

Lack of correlation was found between ventilatory and hemodynamic findings studied simultaneously in 50 patients. Vital capacity was significantly impaired only in decompensated patients. Residual volume was increased in every case of mitral disease. Ventilatory dynamics were also altered in every instance, particularly when congestive heart failure was present. Functional dead space was consistently increased, in spite of an increased alveolar ventilation. These findings confirm that in mitral stenosis the ventilatory perfusion ratio is consistently impaired. Results of postcommissurotomy ventilatory studies were quite variable in spite of good clinical results.

In 26 patients the hemodynamic behaviour was studied before and at varying intervals (30 days to 3·5 years) after mitral commissurotomy. The hemodynamic findings in patients who underwent a successful commissurotomy are similar to those observed in subjects with anatomically and functionally mild mitral stenosis.—[Authors' summary.]

76. **Central Blood Volume, Cardiac Output, and Pulmonary Vascular Pattern in Mitral Stenosis**
K. BRAUN, S. Z. ROSENBERG, and A. SCHWARTZ. *American Journal of Cardiology* [*Amer. J. Cardiol.*] **3**, 40–44, Jan., 1959. 4 figs., 19 refs.

In 50 patients with pure mitral stenosis studied at the Rothschild Hadassah University Hospital, Jerusalem, the cardiac output (C.O.) and central blood volume (C.B.V.) were determined by the dye dilution method with azovan (Evans) blue. Radiographs of the chest, and in 30 cases tomograms of the right lower lung field, were taken and the size of the arteries assessed at the hilum, in the mid-lung, and at the periphery. Six healthy subjects served as controls.

In 11 patients with normal hilar arteries the average C.O. and C.B.V. and the ratio C.B.V.:C.O. were normal. Similarly in 24 patients in whom the size of the hilar arteries was regarded as only moderately increased the average C.O. was normal and there was no significant change in C.B.V. or C.B.V.:C.O. In 15 patients whose hilar arteries were markedly increased in size, however, the average C.O. was significantly reduced and C.B.V.:C.O. increased, the C.B.V. being normal. Analagous results in the opposite sense were obtained on relating the size of the arteries in the mid-lung and at the periphery to the haemodynamic findings. Thus normal and moderately diminished vascular patterns were usually associated with normal values, while markedly diminished vascular patterns were associated with a marked decrease in C.O., an increase in C.B.V.:C.O., and a normal C.B.V. The C.B.V. was about 20% of the C.O. in patients with a normal or moderately altered vascular pattern, and about 25% in those with greatly enlarged hilar and greatly narrowed peripheral arteries.

D. Emslie-Smith

77. **Disturbances in Pulmonary Function in Mitral Stenosis and Left Heart Failure.** [Review Article]
K. W. DONALD. *Progress in Cardiovascular Diseases* [*Progr. cardiov. Dis.*] **1**, 298–308, Feb., 1959. 39 refs.

CORONARY DISEASE AND MYOCARDIAL INFARCTION

78. **Evaluation of the Bilateral Internal Mammary Artery Ligation**
M. S. MAZEL. *Angiology* [*Angiology*] **9**, 353–365, Dec., 1958. 12 figs., 8 refs.

In this paper from the Edgewater Hospital, Chicago, the author describes a series of studies in animals and human beings designed to determine the mode of action and the efficacy of bilateral ligation of the internal mammary artery. In dogs ligation of the internal mammary artery was carried out before ligation of the anterior descending coronary artery; it was found that the animals fared better than those not subjected to mammary ligation. [The numbers involved, however, are too small for any conclusions to be drawn, since only 6 dogs served for experimental and control purposes.] Observations following injection of methylene blue into the mammary artery of dogs revealed the passage of the dye into the myocardium and coronary sinus, but the route was via a meshwork of minute vessels around the pulmonary artery, aorta, and superior vena cava and not directly from the pericardio-phrenic vessels. Perfusion studies in 5 dogs did not show any increase in the "backflow".

Radiographs taken at necropsy after injection of a radio-opaque substance into the internal mammary artery of patients who had died from ischaemic heart disease did not reveal any direct communication between the pericardio-phrenic vessels and the coronary vessels, but the fine meshwork of anastomotic vessels around the base of the great vessels was again opacified.

Of a series of 41 patients subjected to operation, 27 had internal mammary ligation alone and 14 had, in addition, cardiopexy. (The author states that in the

latter operation magnesium silicate was sprayed over the heart and pericardial abrasion carried out.) All the patients had coronary insufficiency. Between 60% and 70% of those subjected to mammary ligation alone obtained relief from angina or substernal discomfort. The addition of cardiopexy carried no greater risk, but gave greater long-term protection by allowing anastomotic vessels to bridge across the granulomatous pericarditis created by the insufflation of magnesium silicate into the pericardial sac.

The author considers that psychogenic factors play an important part in the relief of symptoms, and emphasizes the very great difficulty of assessing the value of any procedure in the average patient subjected to an operation. *W. P. Cleland*

79. **The Relative Incidence of Atherosclerotic Heart Disease in East China and Its Relationship to Cholesterol** TUNG CH'ENG-LANG, WU KUANG-HUEI, and WANG CH'UAN-YANG. *Chinese Medical Journal* [*Chin. med. J.*] **77**, 596–602, Dec., 1958. 13 refs.

To determine the relative incidence of various types of organic heart disease in East China a series of 3,451 patients was studied, 2,198 being "semi-private" patients seen by the authors between January, 1948, and December, 1955, (about 10% in homes or hospitals) and the remaining 1,253 having been admitted to the Shanghai Sixth People's Hospital between May, 1952, and April, 1958. The criteria used for the diagnosis of the various types of cardiovascular disease were those of the New York Heart Association. Rheumatic heart disease accounted for about 50% and hypertensive heart disease for 21% of all cases. Atherosclerotic heart disease accounted for 7% of all cases, for 12·6% of those in patients over 40, and for 17·1% of those in patients over 50. Similar figures for the relative incidence of the various cardiovascular diseases are quoted from several other Chinese centres. The relatively low incidence of atherosclerotic heart disease is contrasted with a figure of 54% found among 127 Caucasian patients with heart disease observed in Shanghai and with an average figure in western countries of about 35%. The incidence of myocardial infarction in the whole series was only 2·8%, while in the hospital there was an average of less than 4 cases a year out of 1,342 medical admissions, of which more than 16% were for heart disease. In this connexion a recent post-mortem study by Hu (published in Chinese) of 816 Chinese and 69 Caucasians with atherosclerosis is mentioned in which it was found that coronary atherosclerosis of the same degree appeared on an average 15 to 20 years later in Chinese than in Caucasian patients.

A study of the serum cholesterol level in 509 healthy Chinese showed that the mean level for 285 men aged 21 to >60 was 155·3 mg. per 100 ml., while for 224 women of the same age group it was 160·5 mg. per 100 ml. Comparable figures for healthy Americans reported by Lawry *et al.* (*Amer. J. Med.*, 1957, **22**, 605) were 231·4 and 229·0 mg. per 100 ml. respectively. In 38 male Chinese patients with myocardial infarction the mean serum cholesterol level was 186·1 mg. per 100 ml., the levels in each age group being 31 to 45 mg. per 100 ml. lower than those in healthy Americans of the same age. The relatively low serum cholesterol level found in Chinese subjects is attributed by the authors to the Chinese diet, in which fats supply less than 15% of the total calories. Indeed, it was this Chinese diet, with its meagre fat content consisting mainly of soya bean and peanut oil, which led Snapper in 1941 to suggest the importance of linoleic and linolenic acids in the prevention of atherogenesis.

Another interesting observation made by the authors was the frequent association of coronary heart disease with hypertension in Chinese patients. Thus of 83 patients with myocardial infarction, 70 had hypertension, and of 95 patients with angina pectoris, all but 6 had a high blood pressure.

[There exists apparently a considerable literature in China dealing with the relationship of atherogenesis to diet and the serum cholesterol level, but this seems to be the first publication in English since Snapper's "Chinese Lessons to Western Medicine" (New York, 1941). It is an interesting coincidence that in investigations on groups of people of three different races, living far apart and with different historical and social backgrounds, virtually the same mean cholesterol level—155 to 160 mg. per 100 ml.—has been found by independent workers. The only common factor between these three groups—Chinese, Bantu, and Yemenite immigrants to Israel—was their diet of low caloric value, of which only about 15% was supplied by fat consisting to a considerable extent of vegetable oils.] *Z. A. Leitner*

80. **Inhibition of Heparin Clearing by Platelets** J. R. A. MITCHELL. *Lancet* [*Lancet*] **1**, 169–172, Jan. **24**, 1959. 4 figs., 18 refs.

After an intravenous injection of heparin a lipolytic substance appears in the blood which increases the translucency of lipaemic plasma and fat emulsions. In experiments carried out at the Radcliffe Infirmary, Oxford, to identify the substance present in normal plasma which inhibits this clearing effect 16 subjects were given a fatty meal containing 75 g. of fat, and venous blood was collected into citrate solution 4 hours later. Half of this was centrifuged at 1,500 r.p.m. for 10 minutes (slow-spun) and the other half at 3,200 r.p.m. for 15 minutes (fast-spun) at room temperature. Six hours after the fat meal 1,500 units of heparin was given intravenously and 5 minutes later a blood sample was taken from the opposite arm and centrifuged at 3,200 r.p.m. for 15 minutes at 2° C. When this plasma was added to the slow-spun and fast-spun specimens of lipaemic plasma the latter cleared much more quickly and completely than the former. Blood was then taken from 11 subjects 4 hours after a similar fatty meal but, after slow-spinning, the supernatant plasma was decanted and then fast-spun for 15 minutes. The deposited plug was shown microscopically to consist largely of platelets. This plug was broken up in a dextrose–acetate–saline platelet-washing reagent, again centrifuged, and finally resuspended in buffered saline. When this substance was added to the clearing system it produced almost the same inhibition of clearing as the slow-spun plasma. Further experiments

were carried out with a cell-free platelet extract and showed that the inhibiting factor was present in the extract and not in the washed platelet debris, that its effect was increased by heating, and that it was not dialysable. Moreover it was shown that the platelet extract could inhibit the clearing of an emulsion of ground-nut oil in water both by heparin-activated plasma and by pancreatic lipase. *C. Bruce Perry*

81. **Alimentary Lipaemia and Heparin Clearing in Ischaemic Heart-disease**
J. R. A. MITCHELL and B. BRONTE-STEWART. *Lancet* [*Lancet*] **1**, 167–169, Jan. 24, 1959. 3 figs., 12 refs.

Alimentary lipaemia and heparin clearing in ischaemic heart disease was studied at the Radcliffe Infirmary, Oxford, in 24 male patients matched in pairs for age, one member of each pair having had a proven myocardial infarction and the other being without evidence of ischaemic heart disease. On the first day each patient was given a standard fatty meal containing 75 g. of fat, blood samples being taken before and at 2, 4, 6, and 8 hours after the meal. The intensity of the alimentary lipaemia was determined by measuring the optical density of the plasma. The patients with ischaemic heart disease had higher optical densities throughout, but particularly at 4, 6, and 8 hours. Samples of plasma obtained after the meal were preserved. On the third day the same patients were given a fat-free meal followed after 4 hours by an intramuscular injection of 1,500 units of heparin; 15 minutes later a blood sample was taken from the other arm. It was then possible to compare *in vitro* the rate of clearing of the lipaemic plasma in four systems. The plasma from a patient with ischaemic heart disease could be cleared by heparin-activated clearing factor from the patient or his control and the plasma from the normal control could be cleared in the same way. There was no significant difference between the four systems in the rate of clearing. The lipaemic samples obtained 2 hours and 6 hours after the fatty meal were of similar optical density, yet the former cleared more rapidly and more completely than the latter, suggesting that the lipid constituents of the plasma must differ physically or chemically at these intervals after a fatty meal. *C. Bruce Perry*

82. **Serum Triglycerides in Coronary Artery Disease**
M. J. ALBRINK and E. B. MAN. *A.M.A. Archives of Internal Medicine* [*A.M.A. Arch. intern. Med.*] **103**, 4–8, Jan., 1959. 7 figs., 22 refs.

Most investigations into the pathogenesis of atherosclerosis and coronary arterial disease in recent years have been based on the hypothesis that an increased serum cholesterol level is a causative factor, and the study of the serum triglycerides and their relationship to the other lipid fractions has been comparatively neglected. This aspect of the problem is considered in the present paper from the Grace–New Haven Hospital (Yale University School of Medicine), New Haven, Connecticut, in which biochemical data from 82 males with a history of myocardial infarction one day to 12 years previously are compared with data from an age-matched control group consisting of 134 subjects with no history of cardiovascular or metabolic disease.

In only 18% of the patients with myocardial infarction was the serum cholesterol level above the arbitrary upper limit of normal accepted by the authors (269 mg. per 100 ml.). But the concentration of triglycerides in the serum was above the upper limit of normal (175 mg. per 100 ml. or 5·9 mEq. per litre) in 70%, the difference between the mean values for patients and controls being statistically significant at the 1% level in the age group 30–39 years and at the 5% level in each decade from 40 to 70. The proportion of the normal population in which the serum triglyceride concentration was above the upper limit of normal rose from about 5% in men of 20–29 years to about 30% in men above 50, whereas in the patients with myocardial infarction the proportion was more than 70% at all ages.

The authors therefore suggest that an error in the metabolism of triglycerides may be the main abnormality in coronary arterial disease. The other findings often reported in this condition, such as an increase in the serum content of cholesterol and low-density lipoproteins and prolonged and intensified alimentary lipaemia, may in their opinion be only secondary to the impaired utilization of triglycerides. *Z. A. Leitner*

83. **Sintrom Long-term Therapy in Angina Pectoris.** [Monograph, in English]
M. WIRECKI. *Cardiologia* [*Cardiologia* (*Basel*)] **33**, Suppl., 1–40, 1958. 17 figs., bibliography.

CARDIOGRAPHY

84. **The Ballistocardiogram in Healthy Subjects and in Patients with Atherosclerosis of the Coronary Arteries.** (Баллистокардиограмма у здоровы хи у больных с атеросклерозом венечных артерий)
A. L. LIMČER. *Терапевтический Архив* [*Ter. Arh.*] **31**, 24–33, Jan., 1959. 4 figs., 39 refs.

The ballistocardiograms of 45 patients aged 41 to 62 with coronary atherosclerosis were compared with those of 53 healthy control subjects aged 20 to 60. There was little difference on the average between the findings in control subjects aged 20 to 40 and in those aged 40 to 60, but the tracings of all the 45 patients showed abnormalities, although at the time only 33 had electrocardiographic changes typical of coronary insufficiency. The most frequent abnormalities were: (1) changes in the size of the different waves—most commonly an increase in G–H and H–I; (2) prolongation of the R–K interval—the " mechanical systole "; and (3) diminution in the size of I–J, with increase in the respiratory oscillations of this wave.

It is concluded that ballistocardiography affords the earliest evidence of coronary atherosclerosis and insufficiency. The findings are independent of the patient's age, but the proportion of abnormal records rises from 4% under the age of 50 to 92% at the age of 80, as might be expected. The changes also reflect the degree of hypertension present. *L. Firman-Edwards*

85. **Ballistocardiographic Changes in Patients with Chronic Non-specific Diseases of the Lungs and Cardiopulmonary Insufficiency.** (Изменения баллистокардиограммы у больных с хроническими неспецифическими заболеваниями легких и легочно-сердечной недостаточностью)
R. M. ZASLAVSKAJA. *Терапевтический Архив* [*Ter. Arh.*] **31**, 34–46, Jan., 1959. 11 figs., 13 refs.

Ballistocardiograms from 65 patients with chronic non-specific pulmonary disease (and cor pulmonale in 23 cases) were compared with those of 16 healthy controls. Of 103 records taken from the 65 patients, the amplitude of all waves was increased in 66, normal in 26, and diminished in 11. Other changes observed were marked respiratory oscillations of I–J, relatively high H and L waves, and prolongation of mechanical systole with retardation of the beginning of this phase in relation to that of electrical systole. Low amplitude was most common in cases of severe pulmonary insufficiency, as was delay in the onset of mechanical systole (indicated by an R–H interval of 0·1 to 0·25 second as against a normal interval of 0·04 to 0·08 second). In 47 out of the 65 cases the ratio K–L:I–J was above the normal average of 1·2, and in 21 the ratio H–I:J–K was 1·2. The ratio J–K:I–J was above the normal maximum of 1·4 in 18 cases. The increase in all these ratios was greater in the presence of pulmonary hypertension. Physical exercise (as in Master's test) often provoked these changes at a stage at which clinical signs of pulmonary strain were not yet manifest. As pulmonary ventilation improved under treatment there was a tendency for the ballistocardiogram to return to normal, as was also noted in cases of asthma after relief of an attack. Ballistocardiography may therefore be usefully employed in the early detection of cor pulmonale. *L. Firman-Edwards*

86. **Ballistocardiographic Changes in the Clinically Healthy after Physical Exercise and Smoking.** (Баллистокардиографические сдвиги у клинически здоровых людей после физической нагрузки и курения)
S. M. GUSMAN and Z. Š. HALFEN. *Терапевтический Архив* [*Ter. Arh.*] **31**, 46–52, Jan., 1959. 5 figs., 16 refs.

Ballistocardiograms were recorded from 50 healthy subjects before and after exercise (12 to 16 ascents of a two-step ladder; height of each step 24 cm.). Changes in the record, chiefly an increase in I–J and a high L wave, were found in 35 cases. Only in 8, however, were the changes of pathological import. Where an abnormality was present in the record before exercise the abnormality was increased after it in all but one case, in which the second record was quite normal. The authors consider that a normal ballistocardiogram after exercise excludes cardiovascular disease, but that an abnormal record without definite pathological changes does not necessarily indicate the presence of cardiac damage.

Similar tests were carried out on 32 subjects before and after smoking one cigarette. Changes in the resting ballistocardiogram after smoking were observed in 17 cases; in 12 these were of little import, but in 5 they were significant. In 3 of these 5 physiological changes and in 2 pathological changes developed after exercise. "Sham smoking" caused no changes. In 3 persons who developed pathological changes after exercise the smoking test did not elicit significant deviations from normal. *L. Firman-Edwards*

SYSTEMIC CIRCULATORY DISORDERS

87. **Treatment of Hypertension with Pentolinium and Mecamylamine**
H. T. N. SEARS, P. J. D. SNOW, and I. B. HOUSTON. *British Medical Journal* [*Brit. med. J.*] **1**, 462–465, Feb. 21, 1959. 12 refs.

We describe our experiences in the control of 78 severely hypertensive patients with pentolinium and mecamylamine extending over 4 years. Side-effects, which occur with both preparations, were more numerous and severe in the case of mecamylamine; in our opinion this outweighed the advantage of its more constant absorption and rendered it unsuitable for long-term use. In some patients the synergistic effect of reserpine enabled the dose of ganglion-blocking agents to be reduced, with a concomitant decrease in the severity of side-effects. Despite the shortcomings of both preparations the results achieved have been most gratifying as regards both the prolongation of life and the restoration and preservation of sight. New ganglion-blocking agents are now available which, from a short acquaintance, seem to offer certain advantages over the older preparations, but it remains to be seen whether they will stand the test of long-term use or be able to improve significantly upon the results already obtained.—[Authors' summary.]

88. **Vasodilatation in the Human Hand. Observations on Primary Raynaud's Disease and Acrocyanosis of the Upper Extremities**
J. H. PEACOCK. *Clinical Science* [*Clin. Sci.*] **17**, 575–586, 1958. 17 refs.

In this plethysmographic study of blood flow to the hands, carried out at the Royal Infirmary, Bristol, vasodilatation was induced in the hands of 30 patients with primary Raynaud's disease, 8 with primary acrocyanosis, and in 12 normal controls; all the subjects were female. The water temperature of a venous plethysmograph was raised to $42 \pm 1°$ C. and this level maintained for half an hour. By means of this technique the capacity of the blood vessels of the hand to undergo vasodilatation was found to be normal in 8 of the patients with Raynaud's disease whose symptoms were mild and who had no disability, but in those with disability the capacity to undergo digital vasodilatation was impaired. In the patients with primary acrocyanosis dilatation was normal. No evidence was found that prolonged mild attacks of digital pallor led to the development of structural disease in the hand or digital arteries. *I. McLean Baird*

Clinical Haematology

89. **Acquired Thrombocytopathy. Observations on the Coagulation Defect in Uremia**
S. F. CAHALANE, S. A. JOHNSON, R. W. MONTO, and M. J. CALDWELL. *American Journal of Clinical Pathology* [*Amer. J. clin. Path.*] **30**, 507–513, Dec., 1958. 2 figs., 24 refs.

A study of the haemorrhagic diathesis which is recognized to occur in renal failure is reported in this paper from the Henry Ford Hospital, Detroit, Michigan. In a previous study (*Thrombosis et Diathesis Haemorrhagica*, 1957, **1**, 433) of the prothrombin consumption time of thrombocytopenic blood the authors had shown that with a one-stage prothrombin consumption technique there was apparently considerable prothrombin left in the serum, but with a two-stage method there was very little residual prothrombin. In uraemic patients with a normal platelet count a similar type of phenomenon was observed. The uraemic platelets showed reduced activity of the lipid component of thromboplastin; this was demonstrated by a thromboplastin generation technique. The activity of the platelets was not increased by rupture following sonic oscillation. When normal platelets were incubated with uraemic plasma there was interference with the lipid thromboplastic component.

A. S. Douglas

90. **A Comparative Study of the Effect of Transfusion of Fresh and Preserved Whole Blood on Bleeding in Patients with Acute Leukemia**
E. J. FREIREICH, P. J. SCHMIDT, M. A. SCHNEIDERMAN, and E. FREI. *New England Journal of Medicine* [*New Engl. J. Med.*] **260**, 6–11, Jan. 1, 1959. 2 figs., 7 refs.

This is a report of a small but carefully controlled clinical trial, using the double-blind technique, of the effect of transfusion of fresh whole blood on bleeding in cases of acute leukaemia. Banked whole blood was used as a control. This was collected in uncoated glass bottles containing acid–citrate–dextrose solution and kept at 5° C. for a period of 2 to 9 days before use. The fresh blood was collected into plastic bags containing sodium calciumedetate (EDTA). Immediately before transfusion the stored blood was transferred to a plastic container to be identical with the fresh blood in appearance. Each of the 9 patients used in the trial received 4 infusions—2 of fresh blood and 2 of stored blood, the type of blood given first being decided by random allocation. There was a minimum interval of 24 hours between each infusion received by the patient. Only visible external bleeding—haematuria, melaena, and epistaxis—was taken into account.

It was concluded that transfusion of fresh blood is more effective in relieving haemorrhage in patients with acute leukaemia than that of stored blood. A favourable response to fresh-blood transfusion was noted in 10 out of 14 cases, whereas of the 14 bank-blood transfusions, only one was followed by a clinical response. The mean rise in platelet count after transfusion of fresh blood was 4,900 per c.mm., and after transfusion of bank blood only 800 per c.mm.

A. S. Douglas

91. **The Removal of Excessive Potassium and Ammonium from Bank Blood prior to Transfusion**
D. C. SCHECHTER, T. F. NEALON, and J. H. GIBBON. *Surgery, Gynecology and Obstetrics* [*Surg. Gynec. Obstet.*] **108**, 1–6, Jan., 1959. 11 figs., 8 refs.

At the Jefferson Medical College of Philadelphia the authors compared the changes in free potassium, sodium, and ammonium content during storage for up to 21 days in blood subjected to three different anticoagulant techniques. Standard 500-ml. specimens of blood were collected as follows: (A) into siliconed vacuum bottles containing 120 ml. of A.C.D. anticoagulant solution (*U.S.P.* Formula B); (B) into plastic bags containing 75 ml. of A.C.D. solution (*U.S.P.* Formula A); and (C) into plastic containers after passage through a cation exchange resin to remove calcium In Group C no anticoagulant was added, and as erythrocyte survival in these circumstances does not exceed 10 days estimations of potassium, sodium, and ammonium content were carried out after 2, 5, and 10 days in this group, whereas in Groups A and B the estimations were made after 7, 14, and 21 days, three specimens being tested on each occasion. After a sample of the specimen had been taken for analysis the remainder of the blood was passed through a column containing 50 g. of " dowex 50–X8 " sodium-cycle resin at a rate of 50 ml. per minute. The analysis was then repeated on a final sample of the blood.

In Group A the plasma potassium content increased to 9·15 to 12 mEq. per litre in 7 days and to 14 to 21 mEq. per litre in 21 days, while the ammonium content rose to 400 to 661 μg. per 100 ml. in 21 days. Final passage through the resin reduced these levels to normal and increased the plasma sodium level, which had fallen during storage, to slightly above normal. In Group B the increase in potassium content was slightly greater (to 10 to 14 mEq. per litre in 7 days and 16·8 to 23·6 mEq. per litre in 21 days), while that in ammonium content was about the same as in Group A. Passage of the stored blood through the resin again reduced potassium and ammonium levels to those of freshly drawn blood and increased the sodium level to slightly above normal. The plasma potassium level in Group C was only 1 to 3 mEq. per litre after the initial passage of the blood through the resin, but it rose rapidly, reaching 9·5 to 12 mEq. per litre in 2 days, although the maximum after 10 days was only 14 mEq. per litre. The ammonium level rose to 380 to 450 μg. per 100 ml. in 2 days and to 520 to 1,250 μg. per 100 ml. in 10 days. Again passage through the resin reduced these levels to normal and increased the sodium level.

Accumulation of potassium and ammonium in the plasma during storage thus occurs to a significant extent

whether anticoagulants are added or decalcification carried out. The infusion of any stored blood may then aggravate the hyperkalaemia resulting from severe tissue damage or renal lesions and may precipitate encephalopathy in patients with portal cirrhosis and other liver diseases. The danger of citrate intoxication as a result of massive blood transfusion will remain so long as A.C.D. mixtures are employed, but the danger from excess potassium and ammonium can be effectively removed by the simple method of passage of the blood through an ion-exchange resin before transfusion.

F. Hillman

ANAEMIA

92. **The Pathogenesis of Anaemia after Partial Gastrectomy. I. Development of Anaemia in Relation to Time after Operation, Blood, and Diet**
I. McL. Baird, E. K. Blackburn, and G. M. Wilson. *Quarterly Journal of Medicine* [*Quart. J. Med.*] **28**, 21–34, Jan., 1959. 7 figs., 34 refs.

The authors present from the United Sheffield Hospitals the results of a clinical and haematological study of the anaemia occurring in 341 patients after partial gastrectomy for peptic ulcer performed between 1940 and 1955. After both the Billroth and the Polya types of operation a progressive fall in the haemoglobin level was found in both sexes, but was observed to be most marked in women under 50—that is, in those still menstruating. Only one case of megaloblastic anaemia occurred in the series, the patient being a man aged 62 with a family history of pernicious anaemia. There was no greater incidence of alimentary bleeding (as judged by tests of faecal occult blood) in patients subjected to partial gastrectomy than in those with peptic ulcer not operated on. The mean dietary iron intake was significantly reduced after operation in men suffering from anaemia, but was not sufficiently low to be the sole cause of the anaemia, suggesting that there is also some fault in iron absorption. In the female patients the dietary intake of iron was generally below the level considered necessary for the maintenance of a normal haemoglobin value. In the majority of patients the response to oral administration of iron, though slow, was satisfactory. *Janet Vaughan*

93. **The Pathogenesis of Anaemia after Partial Gastrectomy. II. Iron Absorption after Partial Gastrectomy**
I. McL. Baird and G. M. Wilson. *Quarterly Journal of Medicine* [*Quart. J. Med.*] **28**, 35–41, Jan., 1959. 20 refs.

In this further study [see Abstract 92] the authors have investigated the efficiency of iron absorption in patients subjected to partial gastrectomy. They recognize that the measurement of iron absorption is difficult, since less than 8% of the iron in the diet is absorbed even by normal subjects and therefore small differences are difficult to measure. They found that the absorption of radioactive iron (^{59}Fe) given as ferrous sulphate to the fasting non-anaemic patient was not affected by partial gastrectomy, nor was the absorption of ^{59}Fe affected when it was incorporated in rabbit's blood and given with a light meal; when the ^{59}Fe was given in rabbit's blood with a full meal, however, there was a significant decrease in absorption. In the anaemic patients there was a slightly enhanced absorption of ferrous sulphate given alone, but no increase when the iron was given in organic combination with food.

It is concluded, therefore, that the pathogenesis of the iron-deficiency anaemia occurring after partial gastrectomy is largely an inability to increase the absorption of iron from the diet in response to need. Haemorrhage and defective or inadequate diet may be contributory factors, especially in younger women still menstruating. *Janet Vaughan*

94. **Refractory Normoblastic Anaemia: a Clinical and Haematological Study of Seven Cases**
J. V. Dacie, M. D. Smith, J. C. White, and D. L. Mollin. *British Journal of Haematology* [*Brit. J. Haemat.*] **5**, 56–82, Jan., 1959. 25 figs., bibliography.

Clinical and haematological data are given of a group of 7 patients suffering from " refractory normoblastic anaemia ". The salient feature of this anaemia is an extremely hyperplastic erythropoietic bone marrow with evidence of both impaired maturation and defective haemoglobin formation, as shown by the cytoplasm of many of the normoblasts being poorly formed and containing excessive numbers of large siderotic granules. The bone marrow of one of the patients was overtly megaloblastic and occasional megaloblast-like cells were present in the bone-marrow films of several of the other patients. Basically, however, erythropoiesis is normoblastic. Both hypochromic and orthochromic red cells are formed. The reticulocyte count is relatively low and normoblasts are most infrequent in peripheral-blood films, except after splenectomy. There is a tendency to mild or moderate leucopenia and thrombocytopenia, but immature leucocytes are virtually absent from the peripheral blood. Studies of iron metabolism, using radioactive iron, and of pigment excretion have confirmed the relative ineffectiveness of erythropoiesis, and it could be shown using radioactive chromium that the red-cell life-span may be impaired to a moderate extent.

Refractory normoblastic anaemia is a chronic disease and no treatment tried, including splenectomy in one patient, had an effect on the course of the disease. Its pathogenesis is unknown. It is possible that it is a very chronic form of erythraemic myelosis, but this cannot be considered as proved. Although there is no positive evidence that refractory normoblastic anaemia is a deficiency disease, it seems that secondary deficiencies of haemopoietic factors such as folic acid, and also perhaps pyridoxine, may accompany it and complicate the clinical and haematological pictures.—[Authors' summary.]

95. **Observations on the Inhibitory Effects of Intrinsic Factor Preparations on Vitamin B_{12} Absorption**
K. B. Taylor, B. J. Mallett, and G. H. Spray. *Clinical Science* [*Clin. Sci.*] **17**, 647–652, 1958. 9 refs.

The authors have studied, at the Radcliffe Infirmary, Oxford, the effects of large doses of intrinsic factor on the absorption of vitamin B_{12} in 7 subjects, some of whom

had pernicious anaemia in remission. These were first given a dose of vitamin B_{12} labelled with radioactive cobalt and the faecal excretion measured; when the experiment was repeated with a large dose of intrinsic factor, inhibition of absorption of the vitamin occurred. In 3 patients out of the 5 in whom inhibition occurred a similar weight of intrinsic factor which had been heated to destroy all intrinsic-factor activity was also shown to inhibit the absorption of vitamin B_{12}, and in 2 of these the inhibition caused by heated intrinsic factor was greater than that caused by unheated intrinsic factor.

The authors conclude that the inhibition of vitamin B_{12} absorption due to large doses of intrinsic factor may result from over-saturation of " intestinal acceptors " or the presence in the intrinsic factor of contaminants with vitamin B_{12}-binding powers. *I. McLean Baird*

96. **Folic Acid and Vitamin B_{12} in Pernicious Anemia. Studies on Patients Treated with These Substances over a Ten-year Period**

J. J. WILL, J. F. MUELLER, C. BRODINE, C. E. KIELY, B. FRIEDMAN, V. R. HAWKINS, J. DUTRA, and R. W. VILTER. *Journal of Laboratory and Clinical Medicine* [*J. Lab. clin. Med.*] **53**, 22–38, Jan., 1959. 3 figs., 44 refs.

From the University of Cincinnati College of Medicine, Ohio, are reported clinical and biochemical observations on patients with pernicious anaemia receiving maintenance treatment for prolonged periods with folic acid or small doses of vitamin B_{12} (cyanocobalamin). Of 36 patients treated for 10 years with folic acid in a dosage of 30 mg. three times a week, only 3 did not eventually show haematological or neurological relapse. The administration of increasing doses of folic acid after each haematological relapse eventually resulted in neurological complications and in marrow hypoplasia. The majority of the patients relapsed during the first 4 years, but those who had been treated earlier with refined liver extracts relapsed later. Patients maintained on vitamin B_{12} given parenterally in an average dose of 0·7 μg. a day retained a satisfactory haematological and neurological status, despite the fact that the level of the vitamin in the serum was consistently below 100 $\mu\mu$g. per ml. The simultaneous administration of folic acid, 5 to 10 mg. per day for one year, to 3 of these patients did not affect the serum vitamin-B_{12} concentration. A further 3 patients showing early neurological changes responded satisfactorily to 7 to 10 μg. of vitamin B_{12} injected parenterally along with 50 mg. of folic acid orally per day. The neurological complications in the remaining patients recovered on a regimen of 5 μg. of vitamin B_{12} plus 50 to 100 mg. of folic acid per day. In the 3 patients who had been satisfactorily maintained on folic acid for several years the serum vitamin-B_{12} level was 30 $\mu\mu$g. per ml. or lower. When these patients were given 1 mg. of vitamin B_{12} parenterally the urinary excretion of folic acid remained unchanged, but that of folinic acid was doubled.

It is concluded that folic acid has no direct effect on the metabolism of vitamin B_{12}. By stimulating bone-marrow activity in pernicious anaemia, however, folic acid forces the utilization of the small amounts of vitamin B_{12} still available, which are thus side-tracked from the central nervous system. Neurological complications then ensue and ultimately the bone marrow becomes exhausted, with continued depletion of vitamin B_{12}. Folic acid metabolism on the other hand is directly affected by vitamin B_{12}; it is suggested that possible mechanisms of action are: (1) stimulation of the formation of N10-formyl tetrahydrofolic acid, (2) conversion of folic to folinic acid, or (3) the releasing of folinic acid from its conjugates. *J. L. Markson*

97. **Studies with Radioactive Vitamin B_{12} after Partial and Total Gastrectomy, with Special Reference to the Production of Intrinsic Factor.** (Untersuchungen mit radioaktivem Vitamin B_{12} bei partieller und totaler Gastrektomie unter besonderer Berücksichtigung der Intrinsic-factor-Produktion)

W. PRIBILLA and H.-E. POSTH. *Schweizerische medizinische Wochenschrift* [*Schweiz. med. Wschr.*] **88**, 1306–1310, Dec. 27, 1958. 7 figs., bibliography.

In an attempt to determine the site of secretion of intrinsic factor the Schilling test was performed on 49 patients who had undergone various types of partial or total gastrectomy for carcinoma (38) or peptic ulcer (11) and on 5 others with inoperable carcinoma of the stomach. Most of the patients were studied at the Surgical Clinic of the University of Cologne. In a control group of normal subjects the mean excretion of radioactive vitamin B_{12} (cyanocobalamin) was 25·6% of the test dose. In 13 subjects who had undergone total gastrectomy it was 0·1%. After a Billroth-II operation the mean excretion of 11 subjects was lower than the mean normal value, but in only 2 cases was the individual value below the lower limit of normal. After other types of partial gastrectomy the values obtained were lower than after the Billroth-II operation, suggesting that the principal site of secretion of intrinsic factor is the body of the stomach, while the antrum produces least. The authors were unable to determine whether the findings after gastrectomy represented an alteration in quality or in quantity of the secretion. They discuss the desirability of replacement treatment with vitamin B_{12} after gastrectomy. *Mary D. Smith*

98. **Vitamin B_{12} Deficiency in Uncharacteristic Macrocytic Anaemia. Comparison of Bone Marrow Findings and Vitamin B_{12} Level in Plasma.** [In English]

H. O. Ø. KRISTENSEN and H. GORMSEN. *Acta medica Scandinavica* [*Acta med. scand.*] **162**, 415–422, Dec., 1958. 12 refs.

At the Geriatric Hospital, Copenhagen, the serum vitamin-B_{12} (cyanocobalamin) level was determined in 40 elderly patients (most of whom had high-colour-index anaemia) and correlated with the bone-marrow appearances. The authors' observation showed that a low serum vitamin-B_{12} level, reflecting a deficiency of this substance, might be present even though the bone marrow did not contain megaloblasts. The findings confirm the view that the presence of large metamyelocytes and hypersegmented leucocytes in the bone marrow is an indication of such a deficiency state. *R. B. Thompson*

Respiratory System

99. **Steroid Therapy in Pulmonary Fibroses**
A. G. W. WHITFIELD. *British Journal of Diseases of the Chest* [*Brit. J. Dis. Chest*] **53**, 28–40, Jan., 1959. 4 figs., bibliography.

The value of steroid therapy in non-tuberculous pulmonary fibroses and infiltrations is examined in the light of personal experience and the published reports of other workers. Pulmonary sarcoidosis responds well in its earlier stages and steroid therapy should be employed in all patients with respiratory symptoms or with progressive or persistent lung lesions. Permanent maintenance therapy is necessary to avoid relapse. Radiation lung damage in the pneumonitis stage appears to respond to steroid therapy and three months' treatment is suggested for all such cases. Long-standing fibrosis shows no response and corticoids are not thought to have any prophylactic value. The Hamman–Rich syndrome is unlikely to respond to steroid therapy, but no other treatment can be offered. The pleural lesions of systemic lupus erythematosus respond dramatically to steroid therapy. The interstitial pneumonitis occurring in this disease shows a less satisfactory response, but both lung and pleural lesions should always be treated with corticoids. Permanent maintenance therapy is required to avoid relapse. The lung lesions of scleroderma are unlikely to be improved by steroid therapy.—[Author's summary.]

100. **The Value of an Index of Maximal Expiratory Force in the Interpretation of Tests of Maximal Ventilatory Capacity**
M. MCGREGOR. *American Review of Tuberculosis and Pulmonary Diseases* [*Amer. Rev. Tuberc.*] **78**, 692–696, Nov., 1958. 6 refs.

The ability to breathe deeply and quickly depends mainly on muscle power and the non-elastic resistance of the lungs, as well as on other factors, including lung compliance, volition, and coordination. Estimates of ventilatory capacity, such as the direct measurement of the maximum breathing capacity (M.B.C.) by maximum voluntary ventilation and the single-expiration measurement of maximum mid-expiratory flow rate (M.M.F.), are often used clinically as indices of the degree of airway resistance. The author of this paper from the Witwatersrand Medical School, South Africa, reports a study in which the maximum expiratory pressure (M.E.P.) which could be maintained on a mercury manometer (with an open glottis for 1 to 2 seconds) following a full inspiration was measured as well as the M.B.C. and M.M.F. in 99 adults of both sexes, including normal healthy entrants to mining and patients with all degrees of pulmonary disability. On these same subjects the expiratory resistance (cm. H_2O per litre per second) was measured by comparison of instantaneous oesophageal pressure with flow at the point during quiet expiration at which pressure to overcome non-elastic resistance was greatest. It was found that both the M.B.C. and the M.M.F. gave a significant correlation with resistance ($r=-0{\cdot}43$ and $-0{\cdot}45$ respectively), but that resistance was better predicted from a regression equation using the ratio of the M.B.C. or M.M.F. to the M.E.P. In this case the correlation between the direct measure of resistance and the ratio was $r=+0{\cdot}59$. *P. Hugh-Jones*

101. **Effects of Aminophylline, Nikethamide, and Sodium Salicylate in Respiratory Failure**
E. K. WESTLAKE and E. J. M. CAMPBELL. *British Medical Journal* [*Brit. med. J.*] **1**, 274–276, Jan. 31, 1959. 1 fig., 10 refs.

The investigation described herein was designed to determine whether respiration could be stimulated chemically. It is pointed out that the patient with an exacerbation of chronic bronchitis is often treated with continuous administration of oxygen, so that hypoxia, which normally stimulates ventilation, does not occur. At the Middlesex Hospital, London, aminophylline, nikethamide, and sodium salicylate were given to a group of 11 patients with chronic bronchitis and emphysema, and the effect of each drug on the partial pressure of carbon dioxide (pCO_2) in the arterial blood was determined.

In 6 patients intravenous injection of 1 g. of aminophylline had no significant effect, but in 3 patients given 8 g. of sodium salicylate intravenously there was a prolonged fall in the pCO_2. The authors point out, however, that the action of sodium salicylate cannot be quickly stopped and the drug has undesirable side-effects. Nikethamide in a dosage of 2·5 to 6·25 g. intravenously produced a fall in the pCO_2 of arterial blood in 3 patients with marked ventilatory failure; the respiratory stimulation ceased within 5 minutes of discontinuing the drug. It is emphasized that the required dose of nikethamide is large and the margin of safety small.
D. Goldman

102. **Studies of Postoperative Lung Volume and Lung Function.** [Monograph, in English]
T. M. SCHEININ. *Annales chirurgiae et gynaecologiae Fenniae* [*Ann. Chir. Gynaec. Fenn.*] **47**, Suppl. 78, 1–130, 1958. 11 figs., bibliography.

103. **Pulmonary Infections Complicating Asian Influenza**
R. G. PETERSDORF, J. J. FUSCO, D. H. HARTER, and W. S. ALBRINK. *A.M.A. Archives of Internal Medicine* [*A.M.A. Arch. intern. Med.*] **103**, 262–272, Feb., 1959. 5 figs., 10 refs.

In October and November, 1957, during the Asian influenza epidemic, 91 patients with pulmonary infections associated with influenza were admitted to the New

Haven Hospital (Yale University School of Medicine), New Haven, Connecticut. There were 53 males and 38 females; 19 of the males were under 40 years and 26 over 50 years old, while 24 of the females were between 16 and 40 years old and 10 of them were pregnant. Of the 91 patients, 40 were negroes. There were 11 deaths.

Examination of the sputum and culture of sputum and blood showed the infection to be bacterial in 38 cases of pneumonia, of which 24 were due to *Streptococcus pneumoniae*, 6 to *Staphylococcus aureus*, and 6 to *Haemophilus influenzae*. Acute tracheobronchitis alone was present in 10 cases and in 43 the aetiology was undetermined. No attempt was made to demonstrate the presence of the influenza virus in every case, but 6 out of 7 patients with pneumonia and all of 7 with non-specific findings on whom haemagglutination inhibition tests were performed had at least a four-fold rise in titre, while the virus was recovered from throat washings from 2 patients and at necropsy in 3 fatal cases. In about half the cases an upper respiratory infection preceded the onset of pneumonia by one week; in the remainder the symptoms of lung involvement appeared concomitantly with those of influenza. The temperature rose to 101° F. (38·3° C.) or higher in 90% of cases, the highest temperatures occurring in cases of bacterial pneumonia. The duration of fever was usually at least 48 to 72 hours. Grossly bloody sputum was regarded as a grave sign, all 5 patients with this symptom dying. Purulent sputum was commonest in cases of pneumococcal pneumonia. Leucopenia was also a grave sign, 5 of 6 patients with a leucocyte count of less than 5,000 per c.mm. dying. Bone-marrow aspiration in 2 of these cases showed leukaemoid arrest. The evidence suggested that pregnant patients and those with heart disease and chronic lung disease were especially susceptible to post-influenzal complications—the series included 10 cases of pregnancy, 11 of heart disease, and 14 of chronic bronchitis. Only a small proportion were chronic alcoholics, in contrast to the experience of this hospital in non-epidemic periods, when the majority of patients admitted with pneumonia are chronic alcoholics. All the patients with bacterial pneumonia received antibiotics (including penicillin, streptomycin, erythromycin, and chloramphenicol), 7 of them dying. Of the 43 patients with pneumonia of undetermined cause, 24 were given antibiotics, although a number [unstated] of the remainder did as well without them.

Of the 11 patients who died, 4 were old and debilitated, with serious chronic disease, but 7 were young, previously healthy adults who died of overwhelming infection of abrupt onset with high fever, toxicity, dyspnoea, bloody sputum, leucopenia, anoxia, and circulatory failure in spite of treatment with antibiotics, oxygen, vasopressor drugs, and adrenal cortical hormones. At necropsy the lungs were heavy and haemorrhagic and " looked more like liver than lung ". Microscopically, the main features were marked haemorrhage, oedema, alveolar necrosis, hyaline membranes, and microscopic abscesses. The adrenal glands appeared normal. The authors speculate on possible additional measures of treatment, especially the use of an extracorporeal heart–lung machine to allow sufficient time for the host's defence mechanisms to come into play, but are nevertheless sceptical of the value of this or any other therapeutic manœuvre in cases with massive lung involvement.

[This paper sheds a useful light on the limited value of adrenal cortical hormones in these fulminating infections.] *I. M. Librach*

104. The Role of Thoracotomy in the Differential Diagnosis of Pleural Effusion

J. M. Schless, H. N. Harrison, and J. A. Wier. *Annals of Internal Medicine* [*Ann. intern. Med.*] **50**, 11–33, Jan., 1959. 5 figs., 4 refs.

The records of 63 patients subjected to thoracotomy for pleural disease at the Fitzsimons Army Hospital, Denver, between 1953 and 1956 have been analysed. On discharge 38 of the patients were considered to have tuberculosis and 25 to be suffering from non-tuberculous pleuritis. The diagnostic reliability of the results of tuberculin skin tests, examination of the pleural fluid, and sputum and gastric analyses is discussed. In none of the ultimately proven cases of tuberculosis was there a negative reaction to the tuberculin skin test; of the cases of non-tuberculous disease, 7 gave a negative reaction to this test. Tubercle bacilli were isolated from the pleural fluid in only 7 cases which were later shown to be tuberculous, indicating that culture of the pleural fluid is not a very reliable diagnostic procedure. The findings on examination of the sputum and/or gastric aspirate were positive at least once in 16 of the tuberculous patients, only 9 of whom had obvious active pulmonary disease.

Decortication was carried out on 57 patients and open pleural biopsy on 6, the pleural and pulmonary tissue removed being subjected to bacteriological and histological examination. Histologically, the pleural changes confirmed the presumptive diagnosis of tuberculosis in 32 of the 38 cases. In 3 additional cases the histological appearance of lesions discovered in the lung at the time of operation established the diagnosis; the authors point out that these additional cases would not have been diagnosed without full open thoracotomy with careful palpation of the lung. The remaining 3 cases, in which the histological findings were negative, are described in detail; in only one of these was there " no reasonable explanation for the disparity ". Bacteriological examination of the resected specimens provided confirmation of the diagnosis in 25 of the 38 cases of tuberculosis. Prolonged preoperative chemotherapy did not appear to affect the histological appearances, but it distinctly lessened the chance of obtaining bacteriological confirmation of the presence of tuberculosis. Thus this retrospective analysis showed that a differential diagnosis of tuberculous from non-tuberculous disease was established in 92% of cases at thoracotomy, a reliability not approached by other diagnostic methods.

Of the 63 patients, 45 were followed up for 6 months to 3½ years. None of those with tuberculosis had a relapse and none of those with non-tuberculous pleurisy developed clinical tuberculosis. *G. Clayton*

Otorhinolaryngology

105. **Skin Diving: Its Physiological and Otolaryngological Aspects**
J. A. FIELDS. *A.M.A. Archives of Otolaryngology* [*A.M.A. Arch. Otolaryng.*] **68**, 531–541, Nov., 1958. 3 figs., 32 refs.

The popularity of the sport of free diving, with or without a self-contained air or oxygen supply, has brought into civilian practice problems which have hitherto been little known outside the fields of naval and aviation medicine and caisson work. According to Boyle's law the volume of a gas varies inversely with the pressure, so that the greater the pressure to which the diver is exposed, the smaller the volume of the air in the lungs. Moreover, according to Dalton's law the solubility of each gas in a mixture such as air is proportional to its partial pressure, so that nitrogen, which makes up 80% of the air, dissolves in the body fluids under increased pressure and is released on return to the surface. If decompression is too rapid intravascular bubbles of nitrogen are formed which block the capillaries, causing anoxia of the tissues. This is the cause of caisson disease or decompression sickness, though usually the quantity of air that the skin diver can carry is too small to allow him to stay down long enough for this complication to develop. The most common complication of skin diving is block of the Eustachian tube with exudation of serous fluid or blood into the tympanic cavity. This is exactly like the aerotitis of aviators, and is treated in the same way. Sinus blockage seems to be less common. The author has seen 5 cases of rupture of the drum in skin divers, all of which healed without trouble. In another case a shallow dive was followed by tinnitus and a hearing loss of 40 db. at 4,000 c.p.s. which has persisted for 2 years and for which no reasonable explanation has been found.

F. W. Watkyn-Thomas

106. **Malignant Lesions of the Nasopharynx**
P. W. SCANLON, K. D. DEVINE, and L. B. WOOLNER. *Annals of Otology, Rhinology and Laryngology* [*Ann. Otol. (St. Louis)*] **67**, 1005–1021, Dec., 1958. 18 refs.

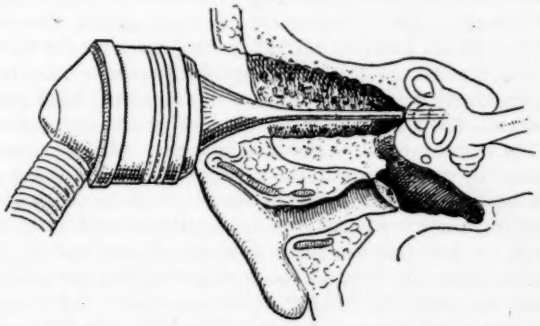
Between 1945 and 1949 88 cases of malignant disease of the nasopharynx were treated at the Mayo Clinic with radium or x rays or both, 19% being cases of squamous-cell carcinoma and 67% of lymphoepithelioma. The patients included both the very young and the very old, the youngest being 5 and the oldest 78. The over-all 5-year survival rate was 17%, and although 67 patients received what would now be regarded as suboptimal dosage, there seemed to be no relation between the survival rate and the amount of irradiation.

In no case in which the floor of the middle cranial fossa was destroyed and the lymph nodes invaded at the same time did the patient survive 5 years.

William McKenzie

107. **The Treatment of Ménière's Disease with Ultrasonic Waves. A Preliminary Report**
F. ALTMANN and J. G. WALTNER. *A.M.A. Archives of Otolaryngology* [*A.M.A. Arch. Otolaryng.*] **69**, 7–12, Jan., 1959. 3 figs., 15 refs.

It has been shown that in animals ultrasonic waves can stimulate the vestibular apparatus, and that repeated or intense stimulation is followed by a complete loss of vestibular responses. In man, however, ultrasonic radiation applied to the outer surface of the mastoid process, even at high intensity, is almost completely absorbed by air and bone and so—except in some patients with sclerotic mastoids—cannot reach the inner ear. Further animal experiments have shown that ultrasound applied at the surface at sufficiently high intensity to reach the inner ear destroys the cochlear as well as the vestibular nerve-endings, so that this method, even if it were applicable to man, would have no advantage over the usual methods of surgical destruction in the treatment of Ménière's disease. Krejci has tried to obviate these difficulties by exposing the wall of the inner ear surgically and using a narrow beam of ultrasonic waves on the wall of the vestibular portion. In one case of Ménière's disease he skeletonized the semicircular canals and irradiated them through a special sound head. Although facial paralysis developed a week after the operation, it had almost completely disappeared after 11 months, while vertigo and tinnitus completely disappeared and there was only a 10-db. loss of hearing. Arslan has improved this method by using a wave-emitter which produces a narrow but intense beam of waves at 800,000 to 1,000,000 c.p.s. and applying it directly to the wall of the horizontal canal (see figure).



No waves can escape to the side of the transmitter, so that further hearing loss and facial paralysis are avoided; nor do the waves seem to reach the inner wall of the petrous or the posterior cranial fossa. The mastoid antrum is opened under local anaesthesia, the horizontal semicircular canal exposed, and the tip of the transmitter applied to the convexity of the canal while an assistant

observes the development and course of nystagmus and at the same time watches for any sign of irritation of the facial nerve.

This technique has been used by the present authors at the Presbyterian Hospital, New York, in 6 cases. In one the hearing improved, while in the others it did not deteriorate. There was complete relief of vertigo and marked improvement in tinnitus in 4 cases. In the other 2 the dose was not enough to destroy vestibular function. Any definite conclusion as to the value of the treatment must, however, await further observation. So far the results have been encouraging, but no patient has yet been followed up for a full year after the treatment, and in Ménière's disease spontaneous remissions may last longer than this.

[The most interesting point in this report is the improvement in tinnitus. After destruction of the labyrinth for Ménière's disease, although there is complete cure of vertigo, tinnitus is likely to persist in most cases. It will be interesting to see whether the hearing survives in the long run; usually when vestibular function is destroyed, as by division of the vestibular nerve, sooner or later hearing goes too, the symptom—vertigo—having been abolished by destruction of the nerve, but the cause —endolymphatic hydrops—remaining unaffected. It is to be hoped that ultrasonic treatment may improve the circulation of the endolymph and thus cure the hydrops.]

F. W. Watkyn-Thomas

108. **Serous Otitis Media in Children**

A. N. LEMON. *A.M.A. Archives of Otolaryngology* [*A.M.A. Arch. Otolaryng.*] **68**, 567–573, Nov., 1958. 9 figs.

Serous otitis media seems to be becoming increasingly common in children in the United States. During 1957 the author saw 116 cases (212 ears), in every one of which the child had been treated for earache within the past year, and always with antibiotics. The diagnosis was based on a history of earache and deafness, on hearing evaluation, and on the appearance of the drum. It is pointed out that unilateral deafness is easily overlooked in such cases, since slight deafness in a child may be mistaken for " inattention ". Audiograms showed a 15- to 30-db. loss over all frequencies, the curve for bone conduction (when tested) being always above that for air conduction. Lack of lustre of the drum head was constant, but a fluid level, air bubbles, and discoloration of the membrane were not always seen. All cases were treated by performing a stab paracentesis in the anterior and posterior aspect of the inferior half of the drum and applying suction at each opening until no more material could be withdrawn. Myringotomy without suction is useless since the fluid is too viscous to flow naturally. Fluid was found in 174 ears, but even with " dry " ears this procedure led to recovery of hearing. In 86 cases adenoidectomy was performed at the same time, and this is recommended as a means of preventing recurrence. In no case were pathogenic organisms found in the fluid. The cell content of the fluid was variable, but no eosinophil leucocytes were found in any case. In 5 consecutive cases in which fluid was present radiographs showed moderate clouding of a normally developed mastoid process. In only a small number of cases was there any evidence of asthma or vasomotor rhinitis.

The author holds that ear drops, nose drops, antihistaminics, antibiotics, sulphonamides, physiotherapy, and Eustachian inflation have no place in the treatment of serous otitis media, and should be condemned. He poses the following questions to which there are as yet no answers: " (1) Does the fluid penetrate the mastoid cells, and, if so, to what extent? (2) Does allergy play a part in aetiology? (3) What happens to the fluid if not evacuated? (4) Is this a collagen disease? "

F. W. Watkyn-Thomas

109. **Secretory Otitis Media in Children**

P. W. THEOBALD. *A.M.A. Archives of Otolaryngology* [*A.M.A. Arch. Otolaryng.*] **68**, 737–747, Dec., 1958. Bibliography.

There is little real evidence that the fluid in the middle ear in secretory otitis media is " secreted " in the proper meaning of the word, at any rate in the early stages. It may be serous or mucoid, or intermediate between the two, and there is still disagreement as to whether it is an exudate or transudate. It is, however, generally agreed that the condition has increased in frequency lately, especially in children, and that the increase is a genuine one and not merely due to greater care in examination. In most cases the exciting cause is recognized to be blockage of the Eustachian tube, though the underlying aetiology is a matter of dispute. Amongst the causes suggested are virus or hypovirus infections, allergy, and the combined effects of low altitude and high humidity, but there is a growing tendency to put the blame on inadequate and irresponsible chemotherapy.

In a series of 50 consecutive children referred for tonsillectomy or adenoidectomy the present author found 12 with secretory otitis media, and his review of the condition is based on his observations in these cases and 25 others encountered during the past year. Diagnosis is made principally by means of the pneumatic otoscope. Fluid levels are seldom seen in children, but amber discoloration of the drum is usual and the movements of the membrane in response to pressure changes are reduced or sluggish. Hearing loss may be difficult to demonstrate in young children, but it is always present, although often unnoticed for a long time. Treatment, when all adenoids have been properly cleared by operation, is by myringotomy. In a few cases mastoid drainage may be necessary. In the author's opinion the recent genuine increase in the incidence of the disease has been due primarily to the frequent and indiscriminate use of antibiotics and secondarily to " extreme conservatism " in recommending adenoidectomy. Reluctance to perform myringotomy is another factor. He holds that irradiation has no place in the treatment of secretory otitis media in children.

F. W. Watkyn-Thomas

110. **Chronic Progressive Deafness, Including Otosclerosis and Diseases of the Internal Ear. Part I.** [Review Article]

B. PROCTOR, E. PICK, M. PORTMANN, and R. BELLUCCI. *A.M.A. Archives of Otolaryngology* [*A.M.A. Arch. Otolaryng.*] **69**, 334–371, March, 1959.

Urogenital System

111. **The Prepubertal Testicular Lesion in Chromatin-positive Klinefelter's Syndrome (Primary Micro-orchidism) as Seen in Mentally Handicapped Children**
M. A. FERGUSON-SMITH. *Lancet* [*Lancet*] **1**, 219–222, Jan. 31, 1959. 2 figs., 14 refs.

The relatively high incidence of chromatin-positive Klinefelter's syndrome in male patients with mental deficiency has been reported by a number of investigators. Determination of the nuclear sex by the oral smear technique of 663 male mentally-handicapped children with an I.Q. ranging from 45 to 85 attending special schools in Glasgow showed that this was female in 8 patients aged 7 to 12 years. All 8 children were prepubertal and 7 of them showed no physical abnormality, but one boy was overweight and only one of his testicles was palpable.

Examination of testicular biopsy specimens from these 8 chromosomal females showed a reduction or absence of germinal cells. In 6 patients the seminiferous tubules were smaller than those of normal controls and contained few spermatogonia, and it was estimated that not more than 20% of the tubules were "fertile". Tubular hyalinization was observed in the oldest patient, aged 12 years. As these changes were already present in the pre-pubertal testis the author suggests that it is reasonable to forecast gross infertility, if not sterility, in these patients, but treatment with androgens might result in normal development of secondary sex characteristics.

R. M. Todd

112. **Autoantibodies in Human Glomerulonephritis and Nephrotic Syndrome**
C. T. LIU and W. W. MCCRORY. *Journal of Immunology* [*J. Immunol.*] **81**, 492–498, Dec., 1958. 3 figs., 40 refs.

The authors, working at the Children's Hospital of Philadelphia (University of Pennsylvania Graduate School of Medicine), examined the serum of children suffering from a variety of diseases for the presence of antibodies to extracts of human kidney. A modification of Boyden's haemagglutination method was used, in which the serum was tested for its ability to agglutinate tanned sheep erythrocytes which had been treated with tryptic digests of human kidney or other tissues. In addition in some cases the serum was tested by Ouchterlony's gel-diffusion method for its ability to produce precipitation from saline emulsions of various tissues.

The haemagglutinin titre of sera from 16 normal children against kidney antigen reached 1:10 in one case only, being less than this in the others. Titres of 1:10 or less were also obtained in all of 7 fatal cases of the nephrotic syndrome, in 11 out of 12 cases of chronic glomerulonephritis, and in all of an unspecified number of cases of miscellaneous renal disease such as pyelonephritis, hydronephrosis, and irradiation nephritis. On the other hand titres of 1:20 to 1:640 or more were obtained in 25 out of 35 cases of acute glomerulonephritis, 48 out of 54 cases of the nephrotic syndrome, 3 out of 10 cases of active rheumatic fever, and 10 out of 14 cases of various infectious diseases such as measles, viral hepatitis, and pneumococcal pneumonia. Sera reacting against kidney antigens also cross-reacted with antigens from human lung, liver, and heart, though usually in a lower titre. Of 14 sera from cases of acute glomerulonephritis tested by the gel-diffusion method, 5 gave precipitin bands with kidney and 3 with liver antigen, while of 11 sera from cases of nephrotic syndrome, 3 gave precipitin bands with kidney, 4 with liver, and one with lung antigen. The presence of these bands showed no correlation with the respective anti-kidney haemagglutinin titres.

The authors point out that these findings are difficult to interpret since the auto-antibodies detected in cases of acute glomerulonephritis and the nephrotic syndrome were not organ-specific and similar auto-antibodies were also found in cases of non-renal disease.

M. C. Berenbaum

113. **Hyperlipemia in Early Stages of Acute Glomerular Nephritis**
W. HEYMANN and S. G. F. WILSON. *Journal of Clinical Investigation* [*J. clin. Invest.*] **38**, 186–192, Jan., 1959. 2 figs., 18 refs.

A marked increase in serum lipid concentration is regularly seen in the nephrotic syndrome, while no such change is thought to occur in acute glomerulonephritis. To investigate this further the serum protein, albumin, cholesterol, and total lipid concentrations have been studied in 111 unselected cases of acute glomerulonephritis in children admitted to the Babies' and Children's Hospital, Cleveland, Ohio. A group of 123 children of similar age not suffering from any condition that might have an effect on serum protein or lipid concentrations served as controls.

Levels of serum protein and albumin lower than any found in the controls were noted in over 20% of the patients with nephritis. The levels were lowest after 2 to 15 days of illness and remained subnormal for up to 23 days. Hydraemia was thought to be responsible. A slight or moderate rise in serum cholesterol level was found in 40% of the nephritic patients, and in total lipid concentration in 43%. The rise started at 2 to 4 days, and reached a maximum at 2 to 4 weeks. Normal values were usually found after one month, but occasionally only after 3 to 8 months. The changes in serum lipid levels were not well correlated with those in serum protein levels and were thought not to be dependent on them, as has been suggested.

David Phear

Endocrinology

114. **Simplified Water Loading Test in Hypoadrenocorticism and Hypothyroidism**
A. M. Moses, J. L. Gabrilove, and L. J. Soffer. *Journal of Clinical Endocrinology and Metabolism* [*J. clin. Endocr.*] **18**, 1413–1417, Dec., 1958. 1 fig., 21 refs.

A water loading test designed for the diagnosis of adrenocortical insufficiency was carried out at the Mount Sinai Hospital, New York, on 15 patients with Addison's disease, 18 with hypopituitarism, and 9 with primary hypothyroidism. The test consisted in measuring the water diuresis resulting from the oral administration of 1,500 ml. of tap water over a period of 15 to 45 minutes after an overnight fast. During the test the patient sat or reclined except when passing urine. Excretion of less than 800 ml. of urine in the 5 hours after the beginning of the test was considered abnormal.

All the patients with Addison's disease, whether treated or not, had an abnormal response, and in all cases an increase in the 5-hour volume of urine was observed when the test was repeated 2 hours after the oral administration of 50 mg. of cortisone, though it did not always exceed 800 ml. Of the 18 patients with hypopituitarism, 13 had hypothyroidism and one was euthyroid, while in the others the thyroid state was not determined. Both before and after cortisone was given the results in these patients were similar to those in the patients with Addison's disease. All the patients with primary hypothyroidism responded normally to the water loading test.

The authors consider that this simple test is valuable in diagnosing the hypoadrenocortical state. It also helps to distinguish primary and secondary hypothyroidism: if there is impaired water tolerance which is improved by treatment with cortisone, then it is likely that the hypothyroidism is secondary to pituitary failure, whereas normal water tolerance is suggestive of primary thyroid dysfunction. *D. G. Adamson*

115. **Thirst-suppressing ("Antidipsetic") Effect of "Pitressin" in Diabetes Insipidus.** [In English]
R. Q. Pasqualini and A. Codevilla. *Acta endocrinologica* [*Acta endocr.* (*Kbh.*)] **30**, 37–41, Jan., 1959. 5 refs.

In 1942 the authors reported 2 cases of diabetes insipidus in which administration of "pitressin" (vasopressin) allayed the sensation of thirst. Since then this action of vasopressin has been studied in 12 cases selected out of a total of more than 50 of diabetes insipidus seen at the Hospital Militar Central, Buenos Aires. The ages of the patients ranged from 3 to 40 years. In one case Hand–Schüller–Christian disease was present and in one there was a pituitary adenoma; in 9 cases the disease was idiopathic and in one it was post-traumatic. Water intake varied from 2·5 litres (in a 4 year-old-child) to 18 litres daily. In all cases polyuria was controlled by posterior pituitary extract or vasopressin.

The patients were deprived of water for a minimum of 8 hours, by which time they were all extremely thirsty and restless. An intramuscular injection of 5 units of vasopressin in aqueous or oily solution was then given. In 7 patients thirst was completely allayed, this suppression and the polyuria lasting from 4 hours in patients given aqueous solution of vasopressin to 36 hours in those given vasopressin tannate in oil. Thirst decreased slightly in 4 patients, while in the remaining patient, a 3½-year-old child, the drug had no effect.

It is suggested that vasopressin suppresses thirst by causing redistribution of water in the body or by a direct action on the nervous centres concerned with perception of thirst. *David Phear*

116. **Ionised, Protein-bound, and Complexed Calcium in the Plasma in Primary Hyperparathyroidism**
H. M. Lloyd and G. A. Rose. *Lancet* [*Lancet*] **2**, 1258–1261, Dec. 13, 1958. 3 figs., 24 refs.

Calcium is present in the plasma in the ionized, complexed, and protein-bound states, the three fractions probably being in equilibrium. In the present study these plasma calcium fractions were measured in 17 patients with primary hyperparathyroidism at University College Hospital, London, in 16 of whom the condition was due to a single chief-cell adenoma, which was removed. The plasma calcium fractions were determined by the chemical method of Rose (*Clin. chim. Acta*, 1957, **2**, 227) before and after the removal of the adenoma in 12 patients and before operation only in the other 5. In one healthy volunteer the same determination was carried out before and after administration of parathyroid hormone.

In 16 of the patients the plasma ionized calcium level was invariably high—the remaining patient being considered to be in temporary remission—whereas that of the protein-bound fraction was normal or only slightly raised. After operation the plasma ionized calcium level fell in all cases to normal or below normal, but the level of the protein-bound fraction either remained unchanged or, in 4 patients, increased. The authors assume that the parathyroid hormone modifies the plasma proteins in such a way as to reduce their ability to bind calcium. This was confirmed by the effect of administering parathyroid extract to the normal subject.

In 2 patients the plasma protein pattern and *p*H were normal and the total plasma calcium concentration was considered to be normal, but the level of the ionized calcium fraction was raised. The authors suggest that this method of measuring the plasma ionized calcium fraction provides a valuable diagnostic test. Thus if in a patient with hypercalciuria the total plasma calcium concentration is normal but that of the ionized calcium

fraction is raised the hypercalciuria is not "idiopathic" and the patient may be suffering from primary hyperparathyroidism. *J. Warwick Buckler*

117. **Development of Hirsutism after Puberty**
F. T. G. PRUNTY, R. V. BROOKS, and D. MATTINGLY. *British Medical Journal* [*Brit. med. J.*] **2**, 1554–1557, Dec. 27, 1958. 1 fig., 21 refs.

The aetiology and diagnosis of post-pubertal hirsutism are discussed with reference to clinical observations in a group of 49 female patients seen at St. Thomas's Hospital, London. The biochemical features of the steroids found in the urine, both with and without stimulation of the adrenal cortex by administration of corticotrophin in a dosage of 20 *U.S.P.* units intramuscularly twice daily for 4 days, are described. Evidence is presented for an increase in adrenal ketosteroid excretion in a large proportion of patients with hirsutism.

G. B. West

118. **Testosterone in Defective Spermatogenesis**
A. W. SPENCE and V. C. MEDVEI. *Lancet* [*Lancet*] **1**, 124–127, Jan. 17, 1959. 12 refs.

An investigation is reported from St. Bartholomew's Hospital, London, of the effect of androgens in the treatment of 30 male patients suffering from defective spermatogenesis. None of the patients had any evidence of general disease and all had normal secondary sexual characteristics and testes which were apparently normal in size. Semen was examined before and at intervals of 1, 2, and 3 months after the start of treatment.

Methyltestosterone was given sublingually in a dosage of 5 to 25 mg. daily for periods of 4 to 16 months to 10 patients with oligospermia. In 7 of these there was no appreciable change in the semen. The wives of 3 became pregnant, and in 2 of these men there was an increase in the sperm count following treatment. To 13 patients (including 5 in the previous group) testosterone propionate was given intramuscularly in a dosage of 50 mg. 3 times a week for 12 weeks. Azoospermia was produced in 6 patients; in only 5 did the sperm count rise above pre-treatment levels. The wives of 6 of these 13 patients eventually became pregnant.

Intramuscular injections of testosterone *iso*butyrate in a dosage of 50 mg. every 4 weeks for 6 months were given to 6 patients, without improvement in the quality of the semen. The wife of one of these patients became pregnant. In 6 patients treatment consisted in subcutaneous implantation of pellets containing 100 to 300 mg. of testosterone. In 2 patients the quality of the semen improved and the wife of one became pregnant. In all, the wives of 11 of the 30 patients became pregnant, but one pregnancy ended in abortion.

The sperm counts of 7 fertile patients ranged from 1 million to 10 million per ml. There was little or no improvement in the quality of the semen as a result of androgen therapy. *Charles Rolland*

119. **The Infant of the Diabetic Mother.** [Review Article]
S. S. GELLIS and D. YI-YUNG HSIA. *A.M.A. Journal of Diseases of Children* [*A.M.A. J. Dis. Child.*] **97**, 1–41, Jan., 1959. 1 fig., bibliography.

THYROID GLAND

120. **The Effect of Thyrotoxicosis on the Electrocardiogram**
G. SANDLER. *British Heart Journal* [*Brit. Heart J.*] **21**, 111–116, Jan., 1959. 36 refs.

A comparative study is presented from the University of Sheffield of the electrocardiograms of 50 thyrotoxic patients before and after treatment with radioactive iodine and of 50 euthyroid control subjects matched for age and sex.

The heart rate in the thyrotoxic patients was significantly increased before treatment and was still higher after treatment than in the control subjects. The average duration of the QRS complex in the thyrotoxic group before treatment was a little prolonged (0·07 second), but fell after treatment to the same level as in the control group (0·06 second). The average height of the R wave in Lead II and in Lead V4 or V5 was greatest in the thyrotoxic group before treatment, was less after treatment, but was still less in the control group. Left ventricular hypertrophy, which was diagnosed if the sum of S in V1 and R in V5 or V6 exceeded 35 mm., was present in 14 thyrotoxic patients and persisted in 5 of them after treatment, but was not present in any of the controls. No cardiomegaly or hypertension was associated with this evidence of hypertrophy, which was attributed to thyrotoxicosis. No change was found in the P wave, P–R interval, Q–T interval, T wave, or electrical axis of the heart in the thyrotoxic group.

J. A. Cosh

121. **Fractionated Plasma Protein Values in Subacute Thyroiditis**
P. G. SKILLERN and L. A. LEWIS. *Journal of Clinical Endocrinology and Metabolism* [*J. clin. Endocr.*] **18**, 1407–1412, Dec., 1958. 14 refs.

From the Cleveland Clinic Foundation, Cleveland, Ohio, the authors report the results of fractionation of the plasma proteins of 27 patients (20 women and 7 men) with subacute thyroiditis. The diagnosis was based on the characteristic history and clinical findings, the results of laboratory tests, and the rapid amelioration of symptoms with prednisone. The plasma proteins were fractionated by Tiselius electrophoresis with Longsworth's modification. A veronal buffer at *p*H 8·6 was used in order to permit the more adequate separation of α_1 and α_2 globulins from albumin.

In 21 of the 27 patients there was an elevation of the plasma α_2-globulin level, and in 19 the fibrinogen level was increased. The erythrocyte sedimentation rate was elevated in 18 out of 20 patients, and in 15 out of 16 of those in whom the α_2-globulin level was increased. In only 6 of 55 patients with Hashimoto's disease and in none of 30 with toxic goitre was there a high plasma α_2-globulin level. The fibrinogen level was above normal in 6 of 35 with Hashimoto's disease who were tested.

The authors suggest that the increase in the plasma α_2-globulin fraction "is caused for the most part by destruction and release of protein from extrathyroidal body tissue consequent to the thyroidal inflammation",

though the liberation of excessive amounts of thyroxine into the plasma may also be a factor. Although an increase in the plasma α_2-globulin level is a non-specific finding, occurring in other diseases, it may provide useful confirmation of the diagnosis of subacute thyroiditis. Nevertheless, the diagnosis of this disease is still best made on the basis of the clinical history, physical findings, response to prednisone or cortisone, and the eventual disappearance of the goitre. *D. G. Adamson*

122. **Simple Physical Concepts in I^{131} Thyroid Uptake and Differential Studies**
M. F. Magalotti and I. F. Hummon. *American Journal of Roentgenology, Radium Therapy, and Nuclear Medicine* [*Amer. J. Roentgenol.*] **81**, 43–46, Jan., 1959. 3 figs.

The authors of this paper from Cook County Hospital, Chicago, review some of the physical aspects of the measurement with Geiger–Müller and scintillation counters of the uptake of radioactive iodine (^{131}I) by the thyroid gland. The merits of the two counters are compared and the method of collimation and the best geometrical design of the collimator discussed. The proper distance of the counter from the patient must be determined by isosensitivity study of the collimator, and the use of a 1/16-inch (1·6-mm.) lead filter to minimize the amount of soft scattered radiation reaching the crystal is recommended. The method of recording is briefly mentioned, and other factors dealt with are the use of a " mock-iodine " reference source for collimation, the importance of background measurements, and the construction of a suitable phantom for dose and standard comparisons. The value of " differential studies "—that is, the comparison of count rates at symmetrical points on either side of the neck— in estimating the ^{131}I uptake of thyroid nodules is discussed, and the importance of correct shielding and collimation is stressed. *K. E. Halnan*

123. **The Effect of Disease and Drugs on the Twenty-four Hour I^{131} Thyroid Uptake**
M. F. Magalotti, I. F. Hummon, and E. Hierschbiel. *American Journal of Roentgenology, Radium Therapy, and Nuclear Medicine* [*Amer. J. Roentgenol.*] **81**, 47–64, Jan., 1959. Bibliography.

The authors review the effects of many different diseases and drugs on the 24-hour uptake of radioactive iodine by the thyroid gland. Typical results obtained in various thyroid diseases are first described, all the common conditions being mentioned, and the effects of radiation and surgery on the findings are detailed. The effects of age, pregnancy, menstruation, and acute haemorrhage are also described, as are those of other endocrine diseases, such as Addison's disease and pituitary tumour, of liver, kidney, and heart disease, and of certain other conditions. Lastly the effect on uptake of various chemicals and drugs is dealt with, including both those known to affect thyroid function, such as antithyroid drugs, thyroid hormones, and pituitary thyrotrophic hormone, and also some others, such as sulphonamides, antihistamines, mercurials, and antibiotics, whose effect is less obvious. *K. E. Halnan*

124. **Importance of the Determination of the Weight of the Thyroid Gland and Clinical Biologic Factors in the Treatment of Hyperthyroidism with I^{131}**
W. Clode, V. Sobral, A. M. Baptista, M. A. Perez-Fernandez, and M. L. Martins. *American Journal of Roentgenology, Radium Therapy, and Nuclear Medicine* [*Amer. J. Roentgenol.*] **81**, 65–73, Jan., 1959. 8 figs., 9 refs.

The authors describe the use of the " pneumothyroid " method of estimating thyroid mass, developed by them at the Portuguese Institute of Oncology, Lisbon, in calculating the dose of radioactive iodine (^{131}I) to be used for the treatment of patients with hyperthyroidism. After an explanation of the formula used in calculating the dose the pneumothyroid technique is described in detail. About 300 ml. of oxygen is injected under the middle cervical fascia as an x-ray contrast medium, so that the outline of the thyroid gland can be seen in radiographs and tomograms taken in two planes at right angles. Thyroid volume is then calculated by means of a formula from measurements of the two lobes as seen on the films.

Treatment with ^{131}I was given to 140 patients with hyperthyroidism between September, 1952, and September, 1957, of whom 117 were followed up, the results in these cases being reported. The calculated radiation dose prescribed varied from 5,000 to 14,000 rads, the average dose at first being 9,600 rads, but being later reduced to 8,300 rads. The thyroid mass was estimated by the pneumothyroid method in 77 of the 117 cases followed up and by palpation in 40. Remission was obtained in 70% and 45% of these two groups respectively, while hypothyroidism developed in 5% and 12·5% respectively. [The time after treatment at which the results were assessed is not stated.] The effects of other factors, such as type and severity of disease, are also analysed. No ill effects from the pneumothyroid technique have been seen in 150 patients investigated.

On the basis of these results it is claimed that the pneumothyroid method of determination of thyroid mass is more accurate than the other methods that are available and that its use in the calculation of the dosage of ^{131}I leads to improved results in the treatment of hyperthyroidism. *K. E. Halnan*

125. **Thyroid Function Assay with Radioiodine: the Correlation of Thyroidal Clearance Factor and Percentage Uptake**
I. Meschan, J. E. Whitley, R. Rogers, and P. S. O'Brien. *American Journal of Roentgenology, Radium Therapy, and Nuclear Medicine* [*Amer. J. Roentgenol.*] **81**, 74–79, Jan., 1959. 5 figs., 1 ref.

At the Bowman Gray School of Medicine, Winston-Salem, North Carolina, two methods of assessing thyroid function with radioactive iodine (^{131}I)—by estimation of the thyroid clearance rate and by estimation of percentage uptake of ^{131}I at one and 2 hours—were compared in 276 consecutive patients. The methods used have been described by Oddie *et al.* (*J. clin. Invest.*, 1955, **34**, 95), the thyroid plasma clearance rate being calculated from corrected measurements of uptake in the neck and

urinary excretion of ^{131}I at given times after the intravenous injection of the test dose.

A log.–log. linear relationship was demonstrated between the thyroid clearance rate at one hour and the percentage uptake both at one hour and at 2 hours. In hypothyroid patients the uptake was less than 3·15% at one hour and less than 4·75% at 2 hours, whereas in hyperthyroid patients the uptake was more than 22·5% at one hour and more than 29·6% at 2 hours. The authors show by statistical methods that the uptake of ^{131}I by the thyroid gland one hour after intravenous injection is closely correlated with the clearance rate, and suggest that determination of thyroid uptake of ^{131}I one hour after intravenous or 2 hours after oral administration of the test dose is as accurate for clinical purposes as is determination of the clearance rate. It is, however, useful to measure uptake in hypothyroid patients 4 or more hours after the dose. *K. E. Halnan*

126. **The Significance of the Protein Bound Radioactive Iodine Determination in Hyperthyroidism.** [In English]
J. S. STAFFURTH and I. BIRCHALL. *Acta endocrinologica* [*Acta endocr. (Kbh.)*] **30**, 42–52, Jan., 1959. 4 figs., 24 refs.

The value respectively of the plasma bound radioactive iodine (P.B. ^{131}I) level and the 24-hour uptake of the isotope by the thyroid gland in the routine diagnosis of thyroid diseases was studied at St. Thomas's Hospital, London.

A P.B.^{131}I level above 0·4% of the administered dose (A.D.) of ^{131}I per litre of plasma at 48 hours, which was considered to be abnormal, was found in all except 4 of the 188 patients eventually considered on clinical grounds to have primary hyperthyroidism. In 3 of the 4 exceptions the 24-hour uptake by the gland was more than 75% of the A.D. In contrast, in all except 2 out of 92 euthyroid patients the P.B.^{131}I level was less than 0·4% of the A.D. One of these 2 patients had subacute nephritis and a high 24-hour uptake of ^{131}I. The authors state that the 24-hour thyroid uptake was much less useful in the diagnosis of primary hyperthyroidism than the P.B.^{131}I level, giving no sharp distinction between normal subjects and thyrotoxic patients. The 6-hour uptake of the thyroid gland was a more reliable guide, as at 24 hours the uptake of a toxic gland may be already past its peak.

^{131}I tests are less useful in the diagnosis of toxic nodular goitre. In 8 out of 22 patients with this type of goitre the P.B.^{131}I level was less than 0·5% of the A.D. and in 2 patients with small, active, symptomless adenomata the P.B.^{131}I level was raised. The 24-hour uptake of the gland is also unreliable in cases of nodular goitre.

After treatment of thyrotoxicosis by surgery or administration of ^{131}I the P.B. ^{131}I level may be raised in euthyroid patients because of a reduction in the organic iodine pool within the thyroid gland. Determination of thyroid uptake at 6 and 24 hours and of the P.B.^{131}I level is therefore necessary in assessing patients after treatment. Similarly, a reduction in the colloidal iodine pool explains the raised P.B.^{131}I level observed in patients with hypothyroidism, whether spontaneous or due to lymphadenoid goitre. *David Phear*

127. **The Measurement of Saliva I^{131} in Percentage of Given Dose per Liter as an Index of Thyroid Function**
L. E. JACOBSON and W. N. MILLER. *American Journal of Roentgenology, Radium Therapy, and Nuclear Medicine* [*Amer. J. Roentgenol.*] **81**, 80–88, Jan., 1959. 3 figs., 13 refs.

Working at the Presbyterian Hospital, Newark, New Jersey, the authors have attempted to assess the value of measurement of the radioactivity of the saliva after the administration of a dose of radioactive iodine (^{131}I) as a test of thyroid function. They gave doses of about 50 μc. of ^{131}I and measured the radioactivity of the saliva (expressed as the percentage of the test dose per litre), plasma inorganic and protein-bound ^{131}I content, and thyroid uptake of ^{131}I after 24 and 72 hours. Of the subjects studied, 32 were euthyroid (16 after thyroidectomy or ^{131}I treatment), 14 were hyperthyroid, and 12 were hypothyroid (4 after thyroidectomy or ^{131}I treatment).

The mean total radioactivity of the saliva at 24 hours was 36% of the dose per litre for the hyperthyroid, 8·8% for the euthyroid, and 1·5% for the hypothyroid patients, and these results are compared with the other findings. It is suggested not only that measurement of salivary ^{131}I concentration is a useful test of thyroid function, but also that " the salivary gland may have a more positive function than that of mere absorption of the iodide radical ".

[The detailed results of all tests are given in the paper in support of this last statement. Unfortunately, the ratio between the inorganic ^{131}I content of saliva and plasma shows wide variations in each group, and particularly in the euthyroid and hyperthyroid groups. The plasma inorganic ^{131}I concentration was probably too small for accurate measurement in some of these cases.] *K. E. Halnan*

128. **Occurrence of Thyroid Nodules in Children following Therapy with Radioiodine for Hyperthyroidism**
G. E. SHELINE, S. LINDSAY, and H. G. BELL. *Journal of Clinical Endocrinology and Metabolism* [*J. clin. Endocr.*] **19**, 127–137, Jan., 1959. 7 figs., 14 refs.

Radioactive iodine (^{131}I) is now rarely used in the treatment of young patients suffering from uncomplicated hyperthyroidism. During the period May, 1945, to July, 1953, a total of 213 patients with toxic diffuse goitre (including 18 who were under 20 years of age) were treated with ^{131}I at the University of California Hospital, San Francisco. Follow-up investigation of these patients 5 to 8 years later showed that nodules had developed in the thyroid gland in 2 out of 5 patients under the age of 10 years at the time of treatment and in one out of 13 patients aged 10 to 20 years at that time. Of the remaining 195 patients, who were over 20 years of age when first treated, nodules developed in 2 only. The evidence suggests that these nodules were true neoplasms. *R. M. Todd*

The Rheumatic Diseases

129. **Rheumatism and Nephritis.** (Rheumatismus und Nierenentzündung)
K. O. VORLANDER, K. W. FRITZ, and H. J. BRAUN. *Münchener medizinische Wochenschrift* [*Münch. med. Wschr.*] **101**, 150–158, Jan. 23, 1959. 2 figs., bibliography.

In this discussion of the incidence of renal involvement in patients with rheumatoid arthritis or rheumatic fever and its complications the authors, from the University Medical Clinic, Bonn, present their own findings and describe some illustrative cases. Out of a total of 78 patients with rheumatic carditis there were 8 cases of renal disease, whereas out of 316 with rheumatoid arthritis only 11 showed such a complication. In the former group all stages of glomerulonephritis as well as focal nephritis were seen, whereas in the latter the usual renal lesion was amyloidosis, nephritis being rare. Some facts and theories regarding the part played by streptococcal infection in the pathogenesis of rheumatic fever and glomerulonephritis are discussed, and the possible role of auto-antibodies is briefly mentioned.

[Although the authors concede the point earlier made by Hartman and Bland (*Amer. J. Med.*, 1951, **10**, 47; *Abstr. Wld Med.*, 1951, **10**, 105) and by other workers that the coincidental occurrence of rheumatic fever and glomerulonephritis is a rare event, they make no attempt to explore the possible theoretical significance of this point in their discussion of aetiology.]

G. Loewi

ACUTE RHEUMATISM

130. **A Controlled Study of *beta* Hemolytic Streptococcal Infection in Rheumatic Families. I. Streptococcal Disease among Healthy Siblings**
J. M. MILLER, S. L. STANCER, and B. F. MASSELL. *American Journal of Medicine* [*Amer. J. Med.*] **25**, 825–844, Dec., 1958. 1 fig., bibliography.

The incidence of Group-A β-haemolytic streptococcal infections in the siblings of rheumatic children was studied at the House of the Good Samaritan, Boston. From September, 1953, to June, 1956, the subjects were seen regularly at 4-week intervals (except during August and September), when a clinical examination was carried out, throat swabs were taken, and blood for determination of the erythrocyte sedimentation rate (E.S.R.) and the antistreptolysin-O titre was withdrawn. After the first 6 months arrangements were made for home visits should acute febrile respiratory attacks occur. When streptococcal infections developed treatment was instituted with buffered potassium penicillin by mouth or with benzathene penicillin by intramuscular injection. The dosage of the former was at first 200,000 units twice a day for 10 days, but it became clear that while this was suppressive it did not eradicate the streptococci; the dose was therefore increased to 400,000 units 3 times a day. Benzathene penicillin was administered in one injection of 600,000 units. Throat swabs were cultured at about 8 to 10, 12 to 14, and 18 to 20 days after the start of treatment. In all, 235 healthy children were observed for a period of 11,839 " person-weeks ". During this period 603 symptomatic respiratory illnesses occurred; 14% of these were associated with β-haemolytic streptococci, 90% of the organisms being of Group A. The commonest respiratory illness was coryza, which was rarely accompanied by evidence of streptococcal infection. The next most frequent illness was tonsillopharyngitis, associated with evidence of Group-A streptococcal infection in 30% of cases. Half of the cases in which the only sign of illness was fever were associated with streptococcal infection. Slightly more than 50% of the infections with Group-A haemolytic streptococci were detected in children who were apparently well. The antistreptolysin-O titre was determined in 76% of all cases of Group-A haemolytic streptococcal infection, a significant rise in the titre being observed in about 40% of both symptomatic and asymptomatic cases. This rise occurred in spite of prompt penicillin treatment. Bacteriological relapse occurred in 30% of patients given the lower dosage of oral penicillin and in 13·8% of those given the higher dosage. The over-all failure rate in patients receiving benzathene penicillin intramuscularly was 9·1%. No definite case of acute rheumatism occurred, but erythema marginatum was detected in one case and rheumatic heart disease in 2, all 3 cases being in children who had not been treated. (In 2 the streptococcal infection was detected only by the subsequent rise in antistreptolysin-O titre and in one there was failure to attend the clinic for two months following a sore throat.) The incidence of haemolytic streptococcal disease was higher in children who still had their tonsils than in those without. The peak periods of haemolytic streptococcal disease were late winter and early spring.

C. Bruce Perry

131. **A Controlled Study of *beta* Hemolytic Streptococcal Infection in Rheumatic Families. II. Penicillin Prophylaxis among Rheumatic Fever Subjects, Comparing Different Regimens**
J. M. MILLER, S. L. STANCER, and B. F. MASSELL. *American Journal of Medicine* [*Amer. J. Med.*] **25**, 845–856, Dec., 1958. Bibliography.

A controlled trial of two methods of penicillin administration in the prevention of β-haemolytic streptococcal infections among children convalescent or completely recovered from acute rheumatic fever was carried out at the House of the Good Samaritan, Boston. Inpatients received 200,000 units of buffered benzylpenicillin by mouth twice a day, a total of 452 patients being observed for 5,136 " person-weeks ". There were

no recurrences of rheumatic fever; there was, however, a " breakthrough " of streptococcal infection in 2 asymptomatic patients, but the carrier state was promptly eradicated by increasing the dose of penicillin to 1·2 million units daily for 10 days. Out-patients were either treated in the same way with oral penicillin (114 patients for 6,545 person-weeks) or were given monthly intramuscular injections of benzathene penicillin (47 subjects treated for 2,498 person-weeks). Among the out-patients receiving oral penicillin there were 26 infections (7 symptomatic, 19 asymptomatic), an infection rate of 4 per 1,000 person-weeks compared with a rate of 14·5 in untreated siblings. There were two recurrences of rheumatic fever, which were attributed to poor patient cooperation. Among patients given long-acting penicillin intramuscularly there were 4 infections (1 symptomatic and 3 asymptomatic); three of these occurred on the 28th day after the injection and one on the 34th day in a patient who had failed to report at the usual 4-week interval. The incidence of streptococcal infection in this group was 1·6 per 1,000 person-weeks compared with 13·9 in the siblings. In 3 of the 452 in-patients a pruritic rash developed, but there were no adverse effects in the out-patients receiving oral penicillin. Reactions to intramuscular injection of benzathene penicillin included varying degrees of pain at the site of the injection (this did not occur with every injection in the same child), occasional local induration with sterile abscess formation, occasional low-grade fever for a day or so following the injection, and hypersensitivity (in 2 cases). *C. Bruce Perry*

CHRONIC RHEUMATISM

132. **A New Pyrazol Derivative in the Treatment of Certain Rheumatic Diseases.** (Un nuovo derivato pirazolica nel trattamento di alcune malattie reumatiche)
A. SCHIAVETTI and L. SCHIAVETTI. *Minerva medica* [*Minerva med. (Torino)*] **49**, 4865–4869, Dec. 26, 1958. 4 figs., 16 refs.

At the Institute of Rheumatology of the University of Rome the authors treated a total of 97 patients aged 13 to 71 years with rheumatoid arthritis (21), degenerative joint changes (30), or non-articular rheumatism (46) with " osadrin ", a preparation consisting of equal parts of 1:4-diphenyl-3:5-dioxypyrazolidine and dimethylaminophenyldimethylpyrazolone with the addition of procaine hydrochloride. The average daily dose was 1 ampoule by injection or 4 to 6 tablets by mouth for 10 to 40 days. [The dose contained in each ampoule or tablet is not stated.]

In a high proportion of cases a significant antirheumatic effect of the treatment was demonstrated locally by diminution of pain, muscular spasm, and exudation, and systemically by disappearance of fever and return to normal of the erythrocyte sedimentation rate. The preparation was well tolerated and there was no local tenderness after injection or gastric upset after oral administration. There was no water retention in spite of increased uric acid elimination.

The authors state that their results confirm those of German workers who have been using osadrin for well over 5 years. *Max Mayer*

133. **Simple, Rapid Diagnostic Test for Rheumatoid Arthritis—Bentonite Flocculation Test**
K. J. BLOCH and J. J. BUNIM. *Journal of the American Medical Association* [*J. Amer. med. Ass.*] **169**, 307–314, Jan. 24, 1959. 3 figs., 16 refs.

A rapid diagnostic aid in rheumatoid arthritis, the bentonite flocculation test, which is a modification of a serological test for the detection of *Trichinella* antibodies, is described in this paper from the National Institutes of Health, Bethesda, Maryland. Bentonite is a naturally occurring clay which is suspended in distilled water. The particles are coated with human gamma globulin, and methylene blue is added to make them readily visible. The particles are then added to drops of serial saline dilutions of the (inactivated) sera to be tested on slides. The result is considered to be positive when at least 50% of the bentonite particles are clumped by a serum diluted 32 times or more, while it is considered to be negative when the particles remain freely suspended.

Positive results were obtained in 97 out of 114 verified cases of rheumatoid arthritis. Results were also positive in 5 out of 11 cases of disseminated lupus erythematosus and 5 out of 10 of scleroderma. Of 58 patients with non-rheumatic arthritis, only 3 gave a positive reaction. Positive reactions to the bentonite flocculation test were obtained in 10% of syphilitic sera as well as biological false-positive sera. *G. W. Csonka*

134. **Bentonite Flocculation Test in Rheumatoid Arthritis**
R. A. DELTORO, R. T. SMITH, K. M. KRON, I. F. HERMANN, and M. H. CLAPPIER. *Journal of the American Medical Association* [*J. Amer. med. Ass.*] **169**, 315–317, Jan. 24, 1959. 12 refs.

The bentonite flocculation test (see Abstract 133) was carried out on sera from 48 patients with definite rheumatoid arthritis, positive results being obtained in 40 instances. A positive reaction was obtained in 4 out of 12 cases of probable rheumatoid arthritis, but only in 3 out of 35 cases of other rheumatic conditions. When the test was performed on sera from 48 patients with various diseases characterized by altered protein metabolism there was a positive reaction in one case only. It is concluded that the bentonite flocculation test is easier and cheaper to perform than other serological tests for rheumatoid arthritis and is a dependable laboratory aid in diagnosis. *G. W. Csonka*

135. **Rose–Waaler Test Using a Rapidly Prepared Serum Fraction**
D. WHILLANS and S. FISCHMAN. *Annals of the Rheumatic Diseases* [*Ann. rheum. Dis.*] **17**, 383–387, Dec., 1958. 23 refs.

From Auckland Hospital, New Zealand, the authors describe the preparation and evaluation of a rapidly prepared γ-globulin fraction for use in the sheep-cell agglutination test for rheumatoid arthritis. The fraction

was prepared by the method of Wolfson *et al.* (*Amer. J. clin. Path.*, 1948, **18**, 723), using ammonium sulphate fractionation, and was compared with the euglobulin fraction prepared by the method of Ziff *et al.* (*Bull. rheum. Dis.*, 1954, **5**, 75) both in the Rose–Waaler haemagglutination test and in the agglutination-inhibition test for comparison. The results of the haemagglutination test with euglobulin and with the ammonium sulphate fraction on 280 sera agreed in 96·1%, the titre being either normal or increased with both fractions, while in the remaining 3·9% the titre was increased with one and normal with the other. Of 100 sera tested by the inhibition method, 51 gave positive and 41 negative results with both fractions, while in 8 cases the results with the 2 fractions disagreed.

The authors consider that their method, employing γ globulin, has the advantage of speed and simplicity. [Similar advantages have recently been claimed by Wiedermann *et al.* (*Z. Rheumaforsch.*, 1958, **17**, 314; *Abstr. Wld Med.*, 1959, **25**, 118) for a test in which euglobulin is used.] *G. Loewi*

136. **Clinical Significance of the Rheumatoid Serum Factor**

J. H. KELLGREN and J. BALL. *British Medical Journal* [*Brit. med. J.*] **1**, 523–530, Feb. 28, 1959. 4 figs., 19 refs.

By correlating the results of estimations carried out during the years 1952–7 of the agglutinating factor or "rheumatoid factor" in the serum of patients with rheumatoid arthritis and related diseases with the clinical findings the authors have attempted to assess the significance of the agglutinating activity of the serum as a diagnostically specific feature. A single serological technique was employed throughout, this being the standard simple modification of the original sheep-cell agglutination test (S.C.A.T.) of Rose. During the period under review 790 patients were admitted to the rheumatism beds of the Manchester Royal Infirmary. Of the 393 with an initial diagnosis of definite rheumatoid arthritis, 87% gave a positive S.C.A.T. result on admission, whereas of 41 with probable rheumatoid arthritis, but in whom an alternative diagnosis had been suggested, only 68% gave a positive result. Among 15 cases of juvenile rheumatoid arthritis (with onset before the age of 15 years), there were 6 (40%) positive results. Positive results were obtained in 51% of 78 cases of diffuse collagen diseases (systemic lupus erythematosus, systemic sclerosis, and periarteritis nodosa), but in only 10% of 229 cases of non-rheumatoid arthritis and in only 4 out of 34 cases of bone diseases and other miscellaneous diseases.

Of the 393 patients with clinically definite rheumatoid arthritis, subcutaneous nodules were present in 39%, and 100% of the 62 males and 92% of the 91 females with nodules gave a positive S.C.A.T. reaction. The proportions were not so high among those who had had the disease for less than one year on admission, even when nodules were present, but in a number of such cases follow-up showed that the original diagnosis of rheumatoid arthritis was incorrect. With the exclusion of these cases, and on the basis of the highest recorded result instead of that of the first test only, a positive S.C.A.T. result was obtained in 96% of males and 92% of females with rheumatoid arthritis. In cases of systemic lupus erythematosus and systemic sclerosis a positive reaction to the S.C.A.T. appeared to be related to the presence of articular or peripheral vascular lesions, or both. In 11 cases of confirmed periarteritis nodosa without rheumatoid arthritis the result was uniformly negative.

Among 1,392 in-patients and out-patients with various polyarthritic syndromes seen during the same period there were 537 cases of ankylosing spondylitis, of which only 4% gave positive S.C.A.T. results, whereas of 129 cases of atypical spondylitis, 12% gave positive results. Some of the latter were later diagnosed as cases of rheumatoid arthritis with major spinal involvement, but a high agglutinating titre was not found to be specially associated with peripheral joint involvement as such, since the majority of 62 cases of psoriasis with an inflammatory erosive polyarthritis gave negative results. The proportion of positive results occurring in cases of other types of arthritis was similarly small. Of 190 patients with uveitis attending the Manchester Royal Eye Hospital, only 10 gave a positive S.C.A.T. result, 6 of whom had concomitant clinical evidence of rheumatoid arthritis.

In the course of epidemiological studies a 1-in-10 random sample of all individuals in the age group 55–64 years in the town of Leigh, Lancashire, was studied. Out of 350 subjects tested, 19 gave a positive S.C.A.T. reaction, of whom 8 were shown to have definite and 4 possible rheumatoid arthritis. Of 94 blood relatives of the 19 propositi, 20% gave positive results compared with 5·7% of a 1-in-30 sample of the adult population (over 25) of the area. It is suggested that the presence of the rheumatoid factor is an index of some inherited metabolic defect predisposing to rheumatoid arthritis and certain other forms of disease that may not yet be fully defined. Conversely, there are a number of forms of erosive polyarthritis not associated with a positive reaction to the S.C.A.T. which need further characterization and investigation, especially in women.

Harry Coke

137. **Report of a Three-year Study on the Systemic and Articular Indexes in Rheumatoid Arthritis. Theoretic and Clinical Considerations**

J. LANSBURY. *Arthritis and Rheumatism* [*Arthrit. and Rheum.*] **1**, 505–522, Dec., 1958. 9 figs., 10 refs.

[The evaluation of the progress of rheumatoid disease is a problem of vital importance to all rheumatologists, and a number of schemes have been devised to that end. Of these schemes, that devised by the author and his co-workers is perhaps the one most worthy of detailed consideration, as being the most complete and "scientific", and this paper should be carefully studied by all rheumatologists.]

A report is presented from Temple University School of Medicine, Philadelphia, on a 3-year study of the value of the systemic and articular indices previously described by the author (*Ann. rheum. Dis.*, 1958, **17**, 101). These are designed to provide an objective and accurate method

of assessment of the inflammatory manifestations of rheumatoid arthritis and the structural changes which accompany them. They are expressed as numerical values arrived at from assessment of such factors as the degree of stiffness, amount of pain and muscle weakness, the total joint inflammation, and the erythrocyte sedimentation rate.

The author considers that a strong case can be made for believing that this method of evaluation will present an accurate record of changes in disease activity. He points out that although the systemic and the articular indices are independently based upon different data, they show nevertheless a significant degree of parallelism in their results, and that these accord closely with the general over-all clinical estimate of changes in disease activity. Before these indices can be recommended for general use he suggests that the matter should be further investigated by a committee of independent observers on a multi-clinic basis. *W. S. C. Copeman*

138. **Side-effects following Triamcinolone**
P. H. KENDALL and M. F. HART. *British Medical Journal* [*Brit. med. J.*] **1**, 682–685, March 14, 1959. 1 fig., 4 refs.

The encouraging initial reports on the use of triamcinolone as a suppressive agent in rheumatoid arthritis have been followed by others suggesting that its therapeutic effect does not differ greatly from that of prednisolone. In this paper from Orpington and Farnborough Hospitals, Kent, the authors report the clinical progress and side-effects observed in 47 patients suffering from rheumatoid arthritis who were maintained on triamcinolone in doses up to 16 mg. daily for periods up to 11 months. The majority were already receiving cortisone or prednisolone, for which triamcinolone was substituted because of a diminished clinical response or the appearance of side-effects. The patients were usually seen at fortnightly intervals, when a full subjective and objective assessment, together with a search for side-effects, was made and the erythrocyte sedimentation rate and serum electrolyte levels estimated, but this was in no way a controlled trial.

In 11 of the 47 cases the drug had to be withdrawn because of rapid deterioration (7 cases) or severe side-effects (4). Altogether side-effects were seen in 24 cases, the commonest being facial and body flushing, which occurred in 17, the appearance of the face being characteristic and distinct from that seen with other steroids. Severe loss of weight occurred in 7 cases and rapid symmetrical muscle wasting in 4, in 3 of which it was predominantly in the legs. Clinical suppression of the symptoms of rheumatoid arthritis was satisfactory, and 36 patients continue to receive triamcinolone in spite of the side-effects in some cases.

It is concluded that there is little to choose between triamcinolone and prednisolone for the treatment of rheumatoid arthritis. The usual side-effects of steroid therapy are certainly not less frequent with triamcinolone and new ones have been seen to develop. The dosage suggested for long-term maintenance therapy is 6 mg. daily. *B. M. Ansell*

139. **Intestinal Perforation and Widespread Arteritis in Rheumatoid Arthritis during Treatment with Cortisone**
R. A. PARKER and P. M. THOMAS. *British Medical Journal* [*Brit. med. J.*] **1**, 540–542, Feb. 28, 1959. 2 figs., 18 refs.

Three cases of intestinal perforation and widespread arteritis in rheumatoid arthritis during treatment with cortisone are described. Most of the few cases of intestinal perforation previously described in patients under treatment with cortisone have had intestinal disease. Widespread acute arteritis is rarely found in rheumatoid arthritis, but since the advent of cortisone therapy such cases appear to have increased. It is suggested that cases of rheumatoid arthritis on cortisone have a greater liability than other diseases to develop an acute arteritis.

We consider that the intestinal perforation and arteritis in the present cases are probably separate abnormal reactions to cortisone which are more likely to occur in cases of rheumatoid arthritis than in other diseases.—[Authors' summary.]

140. **Regression of Amyloidosis Secondary to Rheumatoid Arthritis**
R. A. PARKINS and E. G. L. BYWATERS. *British Medical Journal* [*Brit. med. J.*] **1**, 536–540, Feb. 28, 1959. 3 figs., 26 refs.

Only 2 cases of apparent recovery from amyloidosis secondary to rheumatoid arthritis have been reported; in neither case was there a long follow-up or histological proof of the presence of amyloidosis. In this paper from the Postgraduate Medical School of London and the Canadian Red Cross Memorial Hospital, Taplow, Bucks., the clinical progress of 2 patients with severe generalized rheumatoid arthritis complicated by amyloidosis is described. The first patient, a girl, had had arthritis from the age of 3 years; amyloid disease was diagnosed when she was 8, and during the next 7 years the clinical signs of this disease regressed twice in parallel with remissions of rheumatoid arthritis. When the patient was 15 the nephrotic syndrome developed, unassociated with increased joint activity, and there was some retention of urea, indicating that amyloid deposits had not been absorbed in the periods of clinical improvement. The second patient, a man, developed rheumatoid arthritis at the age of 28 and amyloid disease was diagnosed a year later. Treatment with high doses of cortisone was followed by a remission in both the rheumatoid activity and the signs of amyloid disease. Three years later both conditions relapsed in spite of maintenance therapy with cortisone in a dosage of 50 mg. daily; the dosage of cortisone was then increased to 200 mg. daily, with improvement in both joint activity and the signs of amyloid disease, the improvement being maintained with a dosage of 125 mg. daily. Biopsy examination of the liver and kidney, however, showed that amyloid had not been reabsorbed.

The authors briefly discuss 2 further patients, both females, with amyloidosis secondary to rheumatoid arthritis who were treated with prednisolone. In both patients the dosage needed to suppress the joint symptoms caused peptic ulceration and the drug had to be with-

drawn; no significant changes in the clinical or biochemical state were noted. Triiodothyronine was also given to 2 patients without apparent improvement in the amyloidosis.

The authors conclude that " there does not seem to be any histologically proved case of recovery from amyloidosis secondary to rheumatoid arthritis ". The disappearance of clinical signs does not mean reabsorption of amyloid. Steroid hormones do not appear to influence the disease unfavourably and may have induced remission in 2 of their cases. *K. C. Robinson*

COLLAGEN DISEASES

141. **The Frequency, Prognosis, and Early Diagnosis of Periarteritis Nodosa.** (О частоте прогнозе и ранней диагностике узелкового периартериита)
V. E. LJUBOMUDROV. *Терапевтический Архив* [*Ter. Arh.*] **31**, 50–54, Feb., 1959. 15 refs.

Periarteritis nodosa has been recognized as a disease entity for 90 years, but it is still imperfectly known and, in its *formes frustes*, is very often missed. Consequently its mortality has probably been much exaggerated. An analysis of the records of 1,019 cases from 1866 to 1957 showed that the diagnosis was made during life in only 36% of cases over the whole period, and even in the last 12 years it was established before death in only 42·6%. Of the 368 patients in whom the disease was diagnosed during life, 180 (48·9%) were discharged home substantially improved. Of those diagnosed on clinical grounds, 76·4% died, while among those in whom the diagnosis was made by biopsy the death rate was only 27%, those cases in which diagnosis was based on the histological findings in organs removed at operation occupying an intermediate position with 50% mortality.

It is therefore possible that with the more frequent recognition of mild forms of the disease the mortality would prove to be still lower, since many of these cases evidently undergo spontaneous recovery. Early recourse to biopsy in cases of a general disorder with symptoms implicating a number of organs or systems would probably reveal the incidence of the disease to be higher and its mortality lower than is generally believed at present.
L. Firman-Edwards

142. **Sjögren's Syndrome and Systemic Lupus Erythematosus**
J. M. HEATON. *British Medical Journal* [*Brit. med. J.*] **1**, 466–469, Feb. 21, 1959. 38 refs.

The clinical and pathological features in 28 consecutive cases of Sjögren's syndrome seen at the Bristol Eye Hospital over a period of 9 months are described. The patients, all females, were aged from 35 to 83 years, the majority being over 50. Ocular symptoms, which had been present for 1 to 18 years, consisted in cessation or diminution of secretion from the lacrimal glands. Similar changes were observed in the salivary glands and the submucous glands of the respiratory and upper alimentary tracts. The lacrimal glands showed connective-tissue proliferation and fibrosis, with atrophy of the glandular tissue. In the conjunctiva oedema of the epithelial and subepithelial layers, with marked thinning of the epithelium in the later stages, and destruction of the elastic tissue were observed. The changes in the cornea were similar. In addition to these classic lesions 17 patients had rheumatoid arthritis and a further 9 had arthralgia. Other associated conditions were chilblains or Raynaud's phenomenon or both in 12 cases and leucopenia in 16 and thrombocytopenia in 14 out of 24 cases. Electrophoresis of the serum proteins revealed a lowered albumin level in 15 patients and raised α_2- and γ-globulin levels in 16 and 17 patients respectively. In all cases peripheral blood was examined for the presence of L.E. cells on three occasions at intervals of about 3 weeks, these being found in 10 cases. Mikulicz's disease was present in 2 cases in the series, in both of which L.E. cells were found. Of 2 cases of Felty's syndrome (leucopenia, splenomegaly, and rheumatoid arthritis) one gave a positive reaction to the L.E.-cell test.

In a comparison of the clinical and pathological features of Sjögren's syndrome with those of systemic lupus erythematosus the author finds a number of similarities. He states that L.E. cells are not always found in known cases of systemic lupus erythematosus, nor have they been looked for systematically in cases of Sjögren's syndrome. He suggests that prolonged follow-up of these cases would give further evidence in favour of his hypothesis. *H. F. Reichenfeld*

143. **Intravenous Procaine in the Management of Some Cutaneous Manifestations of Collagen Diseases**
J. FARRINGTON. *Southern Medical Journal* [*Sth. med. J. (Bgham, Ala.)*] **51**, 1426–1431, Nov., 1958. 6 figs., 7 refs.

Procaine has been described as having an anti-histaminic effect, an anti-acetylcholine (nerve-blocking) effect, a direct action on cells (especially nerves and endothelial cells), and an adrenaline-potentiating effect. The results obtained with intravenous administration of procaine in balanitis xerotica obliterans and lichen sclerosus et atrophicus were encouraging, and suggested a trial of this drug in morphoea, acrosclerosis, generalized (systemic) scleroderma, and dermatomyositis, 71 cases of scleroderma of all types and 4 of dermatomyositis being so treated. All the patients were admitted to hospital and given 0·1 g. of " seconal " (quinalbarbitone) by mouth 20 minutes before treatment with procaine started. Initially 500 ml. of 0·1% procaine in normal saline or in 5% glucose solution was given by intravenous drip infusion; if no untoward reaction was observed 1,000 ml. was given once a day for the succeeding 6 days. This course was repeated at intervals of 6 weeks, but if there was no improvement after the third course, treatment was stopped. None of the patients received more than 12 courses or fewer than 3.

From the results the author concluded that intravenous infusion of procaine tended to delay progression of certain cutaneous manifestations of some collagen diseases, especially acrosclerosis with Raynaud's phenomena and peripheral ulceration. *E. W. Prosser Thomas*

Neurology and Neurosurgery

144. **Central Pontine Myelinolysis: a Hitherto Undescribed Disease Occurring in Alcoholic and Malnourished Patients**
R. D. ADAMS, M. VICTOR, and E. L. MANCALL. *A.M.A. Archives of Neurology and Psychiatry* [*A.M.A. Arch. Neurol. Psychiat.*] **81**, 154–172, Feb., 1959. 14 figs., 11 refs.

A curious symmetrical lesion was observed in the pons of 3 patients (2 male and 1 female) suffering from chronic alcoholism and one further patient (female) who was malnourished as the result of severe anorexia, vomiting, and diarrhoea. Two of the alcoholics had symptoms of bulbar palsy and a flaccid quadriplegia; in these the illness ended fatally in 3 to 4 weeks. The pons in both cases showed symmetrical loss of myelin affecting its central three-quarters, and a somewhat lesser destruction of axons and a relative sparing of nerve cells of the pontine nuclei; there was very little secondary degeneration in either case. The third alcoholic died from advanced pulmonary tuberculosis complicated by polyneuropathy. The fourth patient showed no clinical neurological signs. In these last 2 cases there was symmetrical loss of myelin on either side of the midline of the pons, but to a much smaller extent than in the first 2 cases. Again axons and nerve cells were relatively spared. The patient who died from tuberculosis also had evidence of Wernicke's encephalopathy, while the fourth patient showed enlargement of cortical nerve cells such as may be found in pellagra.

The cases are described in considerable detail, but no satisfactory aetiological explanation is offered other than that the change is the result of a nutritional deficiency of an unusual kind. Similarities between this condition and that described by Marchiafava and Bignami in the corpus callosum in the same circumstances are discussed. *J. B. Cavanagh*

DIAGNOSTIC METHODS

145. **The Spike and Wave Complex; a Clinical Correlation**
A. LUNDERVOLD, G. F. HENRIKSEN, and L. FEGERSTEN. *Electroencephalography and Clinical Neurophysiology* [*Electroenceph. clin. Neurophysiol.*] **11**, 13–22, Feb., 1959. 12 figs., 10 refs.

The authors have reviewed 10,000 consecutive electroencephalographic (EEG) recordings taken in the Department of Neurology of the University Hospital (Rikshospitalet), Oslo. Spike-and-wave discharges of some form were discovered in 833 records taken from 363 patients. These spike-and-wave discharges could be classified into 4 groups, depending upon their morphological characteristics. Group A (46 patients) consisted of "classic" paroxysmal discharges at a frequency of 3 per second which were bilaterally synchronous, Group B (119 patients) contained bilaterally synchronous regular discharges at other frequencies or else irregular spike-and-wave activity, in Group C (148 patients) were included appearances similar to those in Group B, but with abnormal activity between the paroxysms, while focal spike-and-wave activity was classified in Group D (50 patients).

Of the 363 patients, only 5% suffered from petit mal epilepsy alone, 17% had major epilepsy only, and 52% had seizures which showed some focal features. The highest incidence of petit mal was found in Group A, but only 20% of patients in this group had petit mal alone. The highest incidence of clinically focal epilepsy was observed in Group D, and the highest incidence of grand mal was in those in whom the EEG revealed an irregular spike-and-wave pattern. But these correlations were by no means invariable and it is thus apparent that the spike-and-wave pattern cannot be regarded as being diagnostic of petit mal, although a significant proportion of patients suffering from this clinical variety of epilepsy show the "classic" spike-and-wave pattern in the EEG. *John N. Walton*

146. **Electromyographic Studies of the Pathological Stretch Reflex. A Contribution to the Measurement of Spasticity in Cerebral Motor Disorders.** (Recherches électromyographiques sur le réflexe d'étirement pathologique. Contribution à la mesure de la raideur dans l'infirmité motrice cérébrale)
J. MENSCH-DECHÊNE, C. MONFRAIX, and G. TARDIEU. *Revue française d'études cliniques et biologiques* [*Rev. franç. Ét. clin. biol.*] **3**, 952–959, Nov., 1958. 3 figs., 5 refs.

The authors, working at the Hôpital de Bicêtre, Paris, have used the electromyograph to study the increase in muscular tone associated with cerebral motor disorders. They used a technique previously employed in similar research upon normal individuals. A modified electroencephalograph was used to record the potentials picked up by surface electrodes 20 to 25 mm. in diameter placed in pairs 4 to 10 cm. apart according to age, one pair on the anterior and one pair on the posterior aspect of the upper arm. Angular movement at the elbow was recorded on the tracing by means of a potentiometer with two arms, one fixed to the upper arm and the other to the forearm so that the axis of rotation coincided with that of the elbow joint. The resistance of the biceps brachialis muscle to passive stretching was measured by a strain gauge in a number of cases.

Studies of spasticity were carried out on 15 biceps muscles in 13 spastic children, and of rigidity on 4 biceps muscles in 3 patients, including 2 children and one adult with Parkinsonism without tremor, while in addition 7 cases of athetoid hypertonicity were examined. The following characteristics of the three states are defined. (1) In spasticity electrical silence is found at rest, and

silence can also be obtained in less than 60 stretchings, provided that these are very slow. Electrical activity is observed with rapid stretching. The speed threshold above which it is impossible to maintain electrical silence can be defined and used to evaluate therapy. (2) In rigidity the electromyographic findings are identical with those observed in spastic muscles. Contrary to previous reports electrical silence occurs both at rest and with very slow stretching, the speed threshold being very low. (3) In athetoid hypertonicity there is often electrical activity at rest. The impulses are irregular and potentials may diminish or disappear during stretching. Electrical silence may occur at times during both rapid and slow stretching. There is no speed threshold.

These findings are compared with previous observations on normal persons, in whom it was found abnormal not to obtain electrical silence in 60 slow or rapid stretchings. The results were also found to be in accordance with those of a dynamometric study of cerebral muscular rigidity previously carried out. The authors claim that both electromyographic and dynamometric tests provide an objective measure of the efficacy of treatment. *Kenneth Tyler*

147. **Electromyographic Studies in Cerebral Palsy**
M. TURNER, M. A. PERLSTEIN, and H. ELAM. *American Journal of Physical Medicine* [*Amer. J. phys. Med.*] **37**, 302–326, Dec., 1958. 19 figs., 34 refs.

Clinically the motor dysfunction in cerebral palsy may be classified as due to: (1) spasticity, (2) dyskinesia (including athetoid movements, rigidity, tremor, dystonia, and ballismus), and (3) ataxia. The study here reported from Cook County Hospital and the Paediatric Department of the Northwestern University Medical School, Chicago, was designed to determine whether cerebral palsy could be classified according to electromyographic (EMG) criteria and whether each of the above types has a characteristic EMG pattern. Emphasis was placed on patterns of movement involving several synergistic muscle groups, since previous studies of single muscles had not been rewarding.

The subjects included 38 patients with cerebral palsy (one with the double lesion of spastic paraplegia and athetoid quadriplegia) and 10 healthy controls. The EMG was recorded by means of an Offner 8-channel ink-writing machine, specially designed surface electrodes placed over the flexor and extensor muscle groups in the proximal and distal segments of the more severely affected limbs being used. In some instances EMG recordings were taken with unipolar or concentric needle electrodes and a Meditron electromyograph. Patients were examined in the supine position and recordings were taken at rest and in response to deep tendon reflexes, cutaneous plantar stimulation, support reaction, crossed nociceptive reaction, synkinetic or associated reaction, and tonic neck reflexes. In 11 patients these procedures were repeated 20 minutes after administration of a muscle relaxant, 5 patients receiving meprobamate intramuscularly and 6 di*cyclo*propyl ketoxime by mouth.

From the findings the authors conclude that characteristic EMG patterns at rest and in response to various stimuli occur in the different clinical types of cerebral palsy. A tentative EMG classification of cerebral palsy is given in the following table.

	Normal and Ataxic	Spastic	Athetoid	Rigidity	Tremors
Rest activity . . .	−	±	++	++*	++†
Spread of deep tendon reflex	−	++	±	+	−
Support reaction . .	−	++	−	+	−
Plantar stimulation response	+	++	±	?	?

* Simultaneously in agonist and antagonist
† Mainly in flexors
− absent; ± present at times; + present constantly; ++ exaggerated

The EMG responses to the crossed nociceptive, synkinetic, and tonic neck reflexes were not of much help in the differentiation of types of cerebral palsy.
Kenneth Tyler

148. **The Electroencephalogram in Kwashiorkor**
G. K. NELSON. *Electroencephalography and Clinical Neurophysiology* [*Electroenceph. clin. Neurophysiol.*] **11**, 73–84, Feb., 1959. 5 figs., 19 refs.

The author of this paper from the National Institute for Personnel Research, Johannesburg, has studied serial electroencephalographic (EEG) recordings taken from 33 African children suffering from kwashiorkor. Serial records were also obtained from 11 apparently normal children and single records were taken from a further 14 patients with kwashiorkor and 27 control subjects. The investigation was prompted by the fact that profound apathy and irritability are commonly encountered in kwashiorkor. Abnormal records were obtained from 36% of the patients suffering from the disease and took the form of excessive slow activity of theta and occasionally of delta frequency in one or both temporal regions. In several cases the abnormality was present only in recordings taken during sleep. Even in cases of kwashiorkor in which the EEG was not significantly abnormal, the dominant rhythms were generally of a lower frequency than those obtained from normal children of comparable age. During recovery from the disease there was generally a striking increase in the frequency of the dominant rhythms and a more normal response to photic stimulation. Although 10 of the 33 patients with kwashiorkor were also anaemic, there was no correlation between the absence or presence and severity of the anaemia on the one hand and the degree of EEG abnormality on the other. The author suggests that the EEG findings favour the possibility that the normal maturation of cerebral rhythms is impeded by kwashiorkor. *John N. Walton*

149. **The Diagnostic Significance of Certain Types of Unilateral Electroencephalographic Activity, Periodic or with a Tendency to Periodicity, in Cases of Cerebral Abscess.** (Importance diagnostique de certaines activités électroencéphalographiques latéralisées, périodiques ou à tendance périodique au cours des abcès du cerveau) J. Le Beau and M. Dondey. *Electroencephalography and Clinical Neurophysiology* [*Electroenceph. clin. Neurophysiol.*] **11**, 43–58, Feb., 1959. 5 figs., 12 refs.

The authors have studied serial electroencephalographic (EEG) recordings taken at the Hôpital Lariboisière, Paris, in 120 cases of organic brain disease in which the clinical diagnosis was subsequently confirmed by operative, post-mortem, or histological (biopsy) findings. This series included 15 cases of brain abscess in one cerebral hemisphere, 4 of subdural empyema, 16 of spontaneous intracerebral haematoma, 26 of post-traumatic haematoma, 16 of cerebral metastases, and 13 of cerebral glioma. The remainder of the patients were suffering from a variety of forms of diffuse brain disease, with no evidence of a space-occupying lesion.

It was found that a unilateral focus of slow activity (usually of delta frequency), which was usually rhythmical in character and showed a typical periodicity of discharge, was almost always encountered in association with lesions which were expanding rapidly. This type of abnormality was discovered in every case of brain abscess; it was comparatively infrequent in cases of cerebral glioma or metastases and was rare in those of intracerebral haemorrhage, occurring in less than 5%. The authors conclude that the type of EEG abnormality may be of considerable value in the diagnosis of cerebral abscess. *John N. Walton*

BRAIN AND MENINGES

150. **The "Dew" Phenomenon of the Brain and Its Relation to the Drainage of the C.S.F. through the Leptomeningeal Canals.** (Феномен «росы» на поверхности мозга и его отношение к оттоку ликвора по каналам мягкой оболочки мозга)
M. A. Baron, F. M. Ljass, and N. A. Maiorova. *Вопросы Нейрохирургии* [*Vop. Nejrohir.*] 3–11, No. 1, 1959. 4 figs., 14 refs.

The authors, working at the Burdenko Institute of Neurosurgery, Moscow, have studied the so-called "dew" phenomenon—that is, the appearance of small droplets of cerebrospinal fluid (C.S.F.) on the surface of the arachnoid in areas of the brain exposed at operation, especially in association with hyperaemia and during epileptic convulsions. A previous study of the anatomical details of the subarachnoid space showed this to consist of two distinct structural elements, C.S.F.-carrying canals and subarachnoid alveoli. In the present experiments the C.S.F. pressure of dogs was increased by the introduction of saline through the cisterna magna after exposing parts of the brain and staining the tissue with trypan blue. The "dew" phenomenon could be readily observed with a dissecting microscope, the droplets appearing first over the C.S.F.-bearing canals and then coalescing and spreading over the adjoining areas. This process could also be elicited by the Queckenstedt manœuvre and the administration of adrenaline.

The authors suggest that transudation of C.S.F. through the arachnoid into the subdural space with subsequent absorption into the dural veins is a physiological process, and is probably the main channel for the drainage of the fluid. The rate of drainage is determined by the permeability of the arachnoid and the gradient of hydrostatic pressure between the subarachnoid space and the dural veins and sinuses. *L. Crome*

151. **Tumors of the Septum Pellucidum and Adjacent Structures with Abnormal Affective Behavior: an Anterior Midline Structure Syndrome**
W. Zeman and F. A. King. *Journal of Nervous and Mental Disease* [*J. nerv. ment. Dis.*] **127**, 490–502, Dec., 1958. 4 figs., 20 refs.

In this paper from Columbus Psychiatric Institute and Hospital (Ohio State University College of Medicine) an account is given of the mental symptoms encountered in 4 patients with neoplasm of the septum pellucidum and adjacent structures. From the evidence presented the authors conclude that a characteristic psychiatric syndrome dominated by abnormal affective behaviour appears to be associated with tumours of the anterior midline structures of the brain. Of the 4 cases described, none was correctly diagnosed on the basis of the clinical findings. One patient was not even suspected of having a cerebral tumour. The mental symptoms in the 4 cases were different, but emotional instability of long duration was a common feature, while confusion and memory defect with confabulation frequently occurred.

[It cannot be said that this paper describes a symptomatology, psychiatric or otherwise, which distinguishes tumours of the septum pellucidum from those of other sites.] *J. MacD. Holmes*

152. **The Immediate Treatment of Non-embolic Hemiplegic Cerebral Infarction**
A. B. Carter. *Quarterly Journal of Medicine* [*Quart. J. Med.*] **28**, 125–140, Jan., 1959. 44 refs.

Cerebral infarction is considered to be a more useful term than cerebral thrombosis since in more than half the cases in which infarction is found post mortem or diagnosed from the clinical symptoms thrombosis cannot be demonstrated. The literature on the relative efficacy in the treatment of cerebral infarction of stellate-ganglion block, vasodilator drugs, corticosteroids, and anticoagulants is reviewed. The author then reports the results obtained in 219 cases of non-embolic cerebral infarction out of a total of 575 cases of apoplexy seen at Ashford Hospital, Middlesex, during 1952 to 1955 inclusive. Cerebral infarction was diagnosed from the clinical findings, haemorrhage being excluded by the symptoms or, in some cases, by the results of lumbar puncture. In 1952 no specific treatment was given and the 54 patients seen in that year served as controls. Of these, 25 recovered and 29 died. A patient was considered to have recovered if he was able to return to a normal way of life with slight or no disability. In 1953

stellate block was performed on 62 patients; the ganglion on the side opposite to the hemiplegia was injected with " xylocaine " (lignocaine) daily for 10 days to produce Horner's sign. Of the 62 patients, 30 improved and 32 became worse or died. In 1954 cerebral vasodilatation by means of carbon dioxide inhalation was tried in 47 patients, of whom 27 improved and 20 became worse or died. Of 56 patients given anticoagulant therapy in 1955, 33 recovered and 23 became worse or died. In this group treatment was with an injection of 12,500 units of heparin followed by two similar injections at 6-hourly intervals. With the first injection of heparin oral anticoagulant therapy was started with phenylindanedione in a dosage of 300 mg. daily, this dosage being reduced as necessary to produce a prothrombin level of 10 to 30% of normal. In patients over the age of 65 two-thirds of this dosage was given. The results obtained with this treatment, especially in patients with strokes of slow, ingravescent onset, were better than those obtained with stellate block or cerebral vasodilatation.

Discussing some of the post-mortem pathological findings, the author states that 14 patients treated by cerebral vasodilatation came to necropsy, 3 of whom had occlusion of a carotid artery. Of the patients given anticoagulants, 12 came to necropsy, and 2 of these had carotid artery occlusion. It was not possible, however, to correlate the pathological findings with the rapidity of onset of symptoms. The author concludes that in cases of cerebral infarction of slow or ingravescent onset anticoagulant therapy appears to be promising.

William Hughes

153. **Prognosis in Subarachnoid Haemorrhage. A Report of 152 Acute Cases.** [In English]
O. Höök. *Acta medica Scandinavica* [*Acta med. scand.*] **162**, 475–492, Dec., 1958. 5 figs., bibliography.

In this report the author discusses the prognosis in subarachnoid haemorrhage with reference to 152 cases admitted to Serafimerlasarettet, Stockholm, within one week of onset (in 90% of cases within 2 days). Of the total number, 72 were referred from medical units and 80 from neurological or neurosurgical units; the author regards this information as important in considering prognosis. The data for the two groups were similar, the only large difference being in the mean age, which was 51·3 years in the medical group and 40·6 years in the neurological group. There was a slight predominance of women (58%). The cause of the bleeding was identified as an arterial aneurysm in 46·7% of the cases, an arteriovenous angioma in 9·2%, and leukaemia in one case; in the remaining 43·4% the cause was undiscovered. On the basis of the estimated risk the patients were divided into four groups: (A1) those in deep coma on admission; (A2) those semi-conscious on admission but usually with severe neurological signs; (B1) those initially in coma but partially or completely recovered from it on admission; and (B2) those without initial coma and partially or completely recovered at the time of admission. Groups A1 and A2 contained 44% of the patients, and of these 59% were over 50 years of age. [It is not clear from the figures how many patients were investigated by angiography.] Necropsy performed in 72 cases revealed an aneurysm in 52, angioma in 2, and no lesion in 18. In a few cases developmental anomalies of the circle of Willis were found, while pulmonary oedema was a common finding.

" Early prognosis " was based on observations during the first 8 weeks from onset. In the first 24 hours the mortality was 12·5%, and in the first week it was 32%. Early prognosis was worst in patients aged over 50. In the various risk groups the mortality in the first 8 weeks was as follows: Group A1, 96%; Group A2, 42%; Group B1, 27%; and Group B2, 20%. A study of late prognosis, that is after 8 weeks, indicated that 25 patients (20%) subsequently died, all but 6 of them from recurrent haemorrhage, the highest fatality rate being in the first year. The over-all mortality for the group was 12·5%. Of the 64 surviving patients followed up, 33 were able to work, 7 had slight symptoms or signs, 14 had moderate symptoms, and 10 were unable to work. In general the prognosis for the 36 patients who received various forms of operative treatment was better than in the remainder, who were treated conservatively.

Brodie Hughes

154. **Subarachnoid Haemorrhage. Prognosis when Angiography Reveals No Aneurysm. A Report of 138 Cases.** [In English]
O. Höök. *Acta medica Scandinavica* [*Acta med. scand.*] **162**, 493–503, Dec., 1958. 4 figs., 25 refs.

A review of the literature on subarachnoid haemorrhage seemed to indicate that the prognosis is better in cases in which angiography revealed no aneurysm than in those in which an aneurysm was demonstrated. The author's own material consisted of 138 cases seen at Serafimerlasarettet, Stockholm, between 1934 and 1955, of which 136 were followed up for an average period of 4·5 years. The sex distribution was equal and the patients' average age was 42·6 years. In 76 cases the patient was not seen until more than 8 weeks after the last haemorrhage and in 33 cases between 2 and 8 weeks after it, so that most of this group had largely recovered from the acute effects of the lesion at the time of admission. Of 29 patients seen within 2 weeks of onset, 13 were comatose or in stupor on admission. Only 9 patients showed severe focal signs, 38 slight or transient signs, and the remainder had no abnormal physical signs. In 80% of cases only one haemorrhage had occurred, in 15% there had been 2, and in 5% three.

Angiograms were not obtained in most cases until at least 3 weeks after the haemorrhage. Vertebral angiography as well as bilateral carotid angiography was performed if there was any clinical indication of a basilar site, and this was present in 38% of the cases. In the light of his experience the author concludes that a negative finding in a bilateral carotid angiogram also constitutes an indication for vertebral angiography. The follow-up, which was largely by postal questionary, revealed that death from recurrent bleeding occurred in 5·8% of the cases. Of the 122 survivors, 80 (67%) were symptom-free and able to work, 27 (22%) had slight symptoms, and 13 (11%) were incapacitated for work (in 4 cases, however, from causes other than the sequelae of the subarachnoid haemorrhage). *Brodie Hughes*

155. **Some Autonomic Concomitants of Ictal Automatism. A Study of Temporal Lobe Attacks**
J. M. VAN BUREN. *Brain* [*Brain*] **81**, 505–528. Dec., 1958. 13 figs., bibliography.

Observations made during 20 seizures on 13 patients subject to epileptic automatism of temporal-lobe origin, with particular reference to changes in autonomic status during these attacks, are reported. The seizures were either spontaneous (7 cases) or induced (by "metrazol" (leptazol) in 7 cases, hyperventilation in 3, and deep stimulation with implanted electrodes in 3). Attacks advancing to a generalized tonic–clonic seizure were not included. Records were made of blood pressure, skin temperature, skin resistance, pulse rate, finger plethysmogram, oesophageal and gastric motility, and respiration. Changes shown during ictal automatism consisted in swallowing movements with an initial fall in skin resistance. Changes in respiration, usually slowing of the rate or temporary arrest in expiration, "appeared at any point during the attack". Paroxysmal bouts of tachycardia occurred later in the attack and were often accompanied by hypertension. Inhibition of gastric peristalsis was often associated with the early stage of an attack. After the seizure the tendency was for all these functions to return to the control level with the exception of skin temperature, which usually rose for several minutes. The changes in autonomic function usually preceded the report of an aura by the patient or the onset of unresponsiveness to command.

Experimental work on human beings and animals in the production of autonomic changes is reviewed. The author states that with the exception of the pulse rate "the changes observed during the automatisms of temporal-lobe epilepsy closely reproduce the alterations in function which result from stimulation of the insula, medial temporal region, posterior orbital, subcallosal and anterior cingulate areas in primates".

The changes in the various autonomic functions during the seizures showed a remarkable lack of interdependence, suggesting that there is a spatial separation in the cortical representation of autonomic function from which the discharge may spread and give rise to a "march" of autonomic changes, and it is possible that this may have a particular value in locating the site of origin of the epileptic discharge. *J. B. Stanton*

156. **Vestibulogenic Seizures. A Consideration of Vertiginous Seizures, with Particular Reference to Convulsions Produced by Stimulation of Labyrinthine Receptors**
S. BEHRMAN and B. D. WYKE. *Brain* [*Brain*] **81**, 529–541, Dec., 1958. 1 fig., 48 refs.

The authors discuss two types of seizure in which a prominent symptom was vertigo (interpreted as a feeling of movement of the patient's body in relation to environment or vice versa). These seizures are divided into two types: (1) those that arise from a local discharge of neurones in the cortical projection zone of the labyrinth in the posterior part of the temporal lobe, and (2) those (rarely observed in clinical practice) in which excitation of receptors in the labyrinth regularly leads to the development of seizures by causing abnormal activity in the reticular formation of the brain stem. For the former type the authors propose the term vestibular seizures and for the second type the term vestibulogenic seizures. The electroencephalographic (EEG) features of these two types of seizure are described, the value of the EEG in the differential diagnosis of the two types being illustrated in the report of a case of vestibulogenic seizures. The clinical differentiation of the two syndromes is outlined, points of difference in the mode of development of the seizure being indicated, and the differential diagnosis from other conditions, such as hypoglycaemia or basilar artery insufficiency, in which vertigo is associated with loss of consciousness is also discussed. *J. B. Stanton*

157. **Nydrane as an Anticonvulsant**
N. KAYE, I. H. JONES, and G. K. WARRIER. *British Medical Journal* [*Brit. med. J.*] **1**, 627–629, March 7, 1959. 7 refs.

A clinical trial is reported of the effect of "nydrane" (N-benzyl-β-chlorpropionamide) as an anticonvulsant in the treatment of 27 patients with epilepsy at the General Infirmary at Leeds and Pinderfields Hospital, Wakefield. The duration of epilepsy ranged from 2 to 50 years, and in general the patients (14 males and 13 females aged 11 to 55 years) had responded poorly to other drugs. Nydrane was given in addition to or as a substitute for other anticonvulsants in a dosage initially of 1 to 1·5 g. daily, increasing to 4 g. daily according to the response. As regards the frequency of convulsions, 3 patients were improved, 6 became worse, and 18 remained unchanged. Administration of the drug did not appear to have any particular effect on the mental state. A generalized morbilliform rash developed in 2 patients and an acute psychotic episode in one, these reactions subsiding when the drug was withdrawn. The authors state that these results differ from those of most previous workers, who found nydrane more beneficial than some other anticonvulsants. The low toxicity of the drug was, however, confirmed. *R. Wyburn-Mason*

158. **The Treatment of Extrapyramidal Hyperkinetic States.** (Die Behandlung extrapyramidaler Hyperkinesen)
H. G. MERTENS and P. A. FISCHER. *Deutsche medizinische Wochenschrift* [*Dtsch. med. Wschr.*] **83**, 2288–2296, Dec. 19, 1958. 4 figs., 17 refs.

Perphenazine ("fentazin"; "trilafon"), a phenothiazine derivative related to chlorpromazine, was given a trial by the authors in the treatment of various hyperkinetic states in patients at the University Neurological Clinic, Hamburg. The drug was given initially intravenously in a dosage of 5 to 25 mg. daily for 2 or 3 days and then orally in a dosage of 16 mg. three times a day.

It was found to be especially effective in Huntington's chorea, one patient who had been many years in hospital being able to go home and manage her housework. Among other hyperkinetic states treated a case of head-nodding and 2 cases of spasmodic torticollis were im-

proved; on the other hand 2 cases of torsion spasm were not benefited. As was expected the drug was of no value in Parkinsonism, since this disorder is primarily a hypokinetic rather than a hyperkinetic state.

G. S. Crockett

NEUROMUSCULAR DISEASES

159. **Dystonia Musculorum Deformans Alleviated by Chemopallidectomy and Chemopallidothalamectomy**
I. S. Cooper. *A.M.A. Archives of Neurology and Psychiatry* [*A.M.A. Arch. Neurol. Psychiat.*] **81**, 5–19, Jan., 1959. 10 figs., 11 refs.

After reviewing the negative results of the medical treatment of dystonia musculorum deformans and of operations on the cortico-spinal tracts in this condition, the author describes the results he has achieved by chemopallidectomy in 16 patients aged 10 to 18 years so treated at St. Barnabas Hospital for Chronic Diseases, New York, over the past 3 years. Of the 16 patients, 13 were relieved of the dystonia on that side of the body for which the operation was performed, bilateral operation in 3 of these cases resulting in bilateral relief; the remaining 3 patients are awaiting operation for the second side. There was one postoperative death in the group. No lasting neurological deficit from the operation was observed in any of the cases. One of the 3 patients who were not benefited by the operation showed some increase in the dystonia postoperatively, but the author was not satisfied with the siting of the operative lesion in this case; in the other 2 cases not benefited at least no adverse effect was produced.

The procedure, which has been previously described (Cooper *et al.*, *J. Amer. Geriat. Soc.*, 1956, **4**, 1208; *Abstr. Wld Med.*, 1957, **22**, 57), consists in first producing a temporary lesion under general anaesthesia by inflation of a small balloon attached to a cannula or by the injection of procaine in the area of the globus pallidus–fasciculus-lenticularis–thalamus group of connexions. In cases in which rigidity and fixed postures are the main features the lesion is first placed in the globus pallidus; if the signs on the side contralateral to the operation are not then relieved a further lesion is produced in the ventrolateral nucleus of the thalamus. When relief is obtained the temporary lesion produced by the balloon is converted into a permanent one by repeated injections of alcohol through the cannula over the course of 7 to 10 days, general anaesthesia not being necessary. A radio-opaque solution may if desired be mixed with the alcohol to enable the exact site of the lesion to be controlled radiographically. Operation for the remaining side may be carried out at a later date. In one of the 5 illustrative cases reported by the author in detail bilateral lesions were produced in the thalamus without apparently causing any sign of mental or physical deficit.

The author states that a lesion in the same situation in different patients does not always produce identical results, and he stresses that the gradual production of the lesion first of all by the balloon and subsequently by alcohol injections constitutes the most efficient and safe method of ensuring that the greatest benefit will follow from the operation. It is noteworthy that all the young patients in this group were of at least average intelligence both before and after operation. Relief in several of the cases in this series has persisted for more than 2 years.

J. B. Stanton

160. **Serum Enzymes. Variations of Activity in Disease of Muscle**
L. P. White. *California Medicine* [*Calif. Med.*] **90**, 1–8, Jan., 1959. 2 figs., 32 refs.

This paper from Stanford University School of Medicine, San Francisco, reports an investigation of the activity of the enzymes aldolase, lactic dehydrogenase (LDH), glutamic-oxalacetic transaminase (GOT), phosphohexose isomerase, and *iso*citric dehydrogenase (ICD) in the serum of 58 patients with various muscular and neuromuscular disorders. The effect of dietary protein supplements on serum enzyme activity and urinary creatine excretion in a number of patients with muscular dystrophy was also investigated, and the enzyme activity in muscle homogenates from dystrophic and healthy mice compared.

In all of 18 boys with pseudohypertrophic muscular dystrophy serum aldolase and LDH activity was abnormally high. Serum phosphohexose isomerase and GOT activity was also increased in about half the cases, but serum ICD activity was normal in all. Serum enzyme activity was highest early in the disease and tended to fall as it progressed, the lowest values being found in the older and most severely crippled patients. The findings were less abnormal in the 9 patients with facio-scapulo-humeral muscular dystrophy. In no case was the serum GOT or phosphohexose isomerase activity increased and in only one was there an increase in LDH activity; on the other hand serum aldolase activity was high in all save 2 elderly women. Six dystrophic patients in various stages of their disease were studied intensively while receiving extra dietary protein, either orally or intravenously. In no case was there any improvement in muscle strength or change in serum enzyme activity or urinary creatine output. This was in contrast to previous findings in a patient with muscular wasting due to cancer.

In 9 patients with dermatomyositis serum enzyme activity correlated well with the severity of muscle damage, and from observations made in 2 of these cases it is suggested that an early fall in the serum enzyme values is an indication of efficacy of therapy. In 22 patients with other neuromuscular disorders, including myotonia dystrophica, amyotonia congenita, myasthenia gravis, Parkinsonism, primary lateral sclerosis, and cerebellar ataxia, the serum enzyme activity was within the normal range. Increased serum LDH activity was found in 6 out of 8 patients with recent cerebral vascular accidents; the values for aldolase and GOT were not abnormal, but phosphohexose isomerase activity was increased in the 2 cases in which it was estimated.

A decrease in aldolase and LDH activity and an apparent increase in that of ICD were found in muscle homogenates from dystrophic mice as compared with those from healthy litter-mates.

Celia Oakley

Psychiatry

161. **Menstruation and Acute Psychiatric Illnesses**
K. DALTON. *British Medical Journal* [*Brit. med. J.*] **1**, 148–149, Jan. 17, 1959. 5 figs., 3 refs.

In this paper from University College Hospital, London, an investigation is reported of the relationship between acute psychiatric illness in women and the phase of the menstrual cycle. The admission records of two large mental hospitals (with a total of nearly 5,000 beds) and the mental observation ward of a London teaching hospital were examined, and in respect of women admitted on the grounds of urgency the date of the last menstrual period at the time of admission was noted. For purposes of the investigation the menstrual cycle was divided into seven 4-day periods, days 1 to 4 corresponding to menstruation and days 25 to 28 to the premenstruum. The author states that although menstruation may exceed 4 days, the full flow with relief of water retention is usually covered by the first 4 days. Reliable information was obtained in respect of 276 patients.

The findings emphasized the importance of the premenstrual and menstrual periods in the onset of acute psychotic episodes: 46% of the patients were admitted during this time, as were 53% of those who attempted suicide, 47% of those with depression, and 47% of patients with schizophrenia. This influence of menstruation was observed in about equal numbers of single, married, and widowed patients, nulliparous and multiparous women, and those admitted for first and for recurrent attacks. There was, however, a marked difference in age distribution, the disturbing influence of menstruation being greatest in patients under 25 years.

The author states that the significance of these figures lies in the immediate prognostic value. Patients seeking psychiatric help in the premenstruum may be expected to become worse up to the fourth day of the menstrual cycle, unless premenstrual tension is treated. She emphasizes that premenstrual tension can be successfully treated and that hormone therapy is not contraindicated by psychiatric treatment.

[This is a lucid and significant piece of work.]

R. J. Matthews

162. **The Role of Emotional and Allergic Factors in Hay Fever**
L. REES. *Journal of Psychosomatic Research* [*J. psychosom. Res.*] **3**, 234–241, Jan., 1959. 10 refs.

An investigation was carried out at the Asthma and Allergy Clinic, St. David's Hospital, Cardiff, to determine whether: (1) patients suffering from hay-fever exhibit specific personality features, (2) hay-fever patients as a group differ from a comparable control group in the incidence of psychoneurotic symptoms, and (3) emotional changes play a relevant part in hay-fever either at its onset or subsequently, the subjects being 50 hay-fever patients selected at random and a control group of 50 patients, matched for age and sex, who had been subjected to herniotomy or appendicectomy. The diagnosis of hay-fever was based upon an accurate history, with special reference to the seasonal incidence of symptoms, the results of examination of the nose and nasal smears, the blood count, and the response to skin tests. For each patient and control a total of 200 items relating to social and family history, personal history, personality, and clinical and laboratory findings, were collected, transferred to a punch-card system, and analysed. Age at onset of hay fever ranged from infancy to old age, but two-thirds of the patients were under the age of 25.

No specific personality traits were found in the hay-fever group, although these patients displayed a tendency to be excessively anxious, ambitious, and obsessional. The incidence of anxiety and tension was significantly higher in hay-fever patients than in the controls. In 5 of the former there was onset of symptoms in association with severe emotional stress, while in a further 13 emotionally charged events precipitated hay-fever symptoms at a later stage. The incidence of psychoneurotic traits and symptoms was higher in the patients in whom the symptoms were provoked by emotional changes than that in other hay-fever patients. In a number of patients in whom rhinitis became perennial, emotional factors played as important a part as allergy and infection.

These findings indicate that emotions may influence the reactivity of the nasal mucosa to pollens, and it is probable that nasal hyperfunctioning induced by emotional tension is mediated by parasympathetic pathways. Clinically, it is important to regard the hay-fever patient as a whole, taking into account psychological as well as physical aspects of the condition.

A. Balfour Sclare

163. **Natural History of the Psychoneuroses**
H. E. R. WALLACE and M. B. H. WHYTE. *British Medical Journal* [*Brit. med. J.*] **1**, 144–148, Jan. 17, 1959. 6 refs.

The " natural history " of a mental disorder is defined as the course of the illness when uninfluenced by any treatment, the latter being interpreted here as " any formal psychotherapy given by a psychiatrist ". The University Department of Psychiatry in the General Infirmary at Leeds was opened in 1946, and the demands on its services were so great that by 1955 a total of 83 patients still awaited treatment, some of them having waited 7 years. The natural history of all in this group for whom valid information could be obtained was analysed; some patients were reluctant initially to respond to the inquiry, but eventually informative histories were available in respect of 49 of the 83 patients.

It was estimated that 25 had suffered from anxiety states, 12 from hysteria, and the remaining 12 from

miscellaneous syndromes. Nearly two-thirds had recovered spontaneously or were sufficiently recovered to be working full-time without loss in socio-economic status, 13 had not improved, and 4 were dead. Those who recovered tended to have more stable marriages and more satisfying group relationships than those who failed to recover. Spontaneous recovery was usually complete by the third year. Reluctance to reply to the inquiry had no apparent connexion with the passage of time, the degree of recovery, or the fact that no treatment had been received. *R. J. Matthews*

164. **The Physical Development of Mongols**
G. DUTTON. *Archives of Disease in Childhood* [*Arch. Dis. Childh.*] **34**, 46–50, Feb., 1959. 6 figs., 17 refs.

At St. Lawrence's Hospital, Caterham, the author has studied the physical development of mongol boys in terms of height and skeletal maturation, as assessed from radiographs of one hand and wrist. [The number studied is not stated.] Skeletal maturation was predominantly normal according to the standards of Grenlich and Pyle (*Radiographic Atlas of Skeletal Development of the Hand and Wrist*, Stanford, California, 1950). On the other hand all the mongol boys examined were retarded in linear growth by comparison with the mean values for school-children in the County of London.
R. S. Illingworth

165. **Trifluoperazine Dihydrochloride (" Stelazine ") in Paranoid Schizophrenia**
R. MACDONALD and T. P. S. WATTS. *British Medical Journal* [*Brit. med. J.*] **1**, 549–550, Feb. 28, 1959. 5 refs.

The authors report from Holloway Sanatorium, Virginia Water, Surrey, a trial of trifluoperazine dihydrochloride (" stelazine ") in two groups of patients: (A) 30 male chronic paranoid schizophrenics who had been in hospital for at least 2 years and had been treated without success by various methods, and (B) 20 with acute paranoid schizophrenia of less than 6 months' duration to whom no previous treatment had been given. The treatment regimen consisted in giving 5 mg. of the drug daily for 3 days, this dose being increased by 5 mg. daily every subsequent 3 days until satisfactory results or gross side-effects were seen. The maintenance dose which caused no side-effects but produced maximum therapeutic effect was calculated to vary from 5 to 20 mg. daily. The maximum therapeutic dose of the drug used in this trial was 45 mg. per day.

Before treatment only 4 patients in Group A had been able to adjust to social living in the hospital community (including outings on parole and short home leaves), whereas during treatment 12 were able to do so and 9 were discharged from hospital, 5 being able to return to full employment. Of the 20 patients in Group B, 14 were discharged and were able to return to full employment. All have been out of hospital for 5 to 9 months, and no patient has relapsed while taking the drug. It was noted that in both groups the greatest effect was on aggression and over-activity, next greatest on auditory hallucinations and delusions, and the least effect on ability to concentrate, sustained or abstract thinking, and on comprehension; insight often returned. Normally the improvement was gradual. The only side-effects noted were drowsiness, Parkinsonian symptoms, motor restlessness, and increased salivation. The administration of benzhexol hydrochloride, 6 to 8 mg. daily, eliminated the Parkinsonism and decreased the restlessness; drugs such as amphetamine, barbiturates, and antihistamines were of no avail. A comparison with 24 similar cases given insulin coma treatment showed that for these patients the average stay in hospital was 23½ weeks, whereas for the two trial groups it was only 12½ weeks. The percentage of patients returning to full employment was also higher amongst those receiving treatment with trifluoperazine. *G. de M. Rudolf*

166. **A Study of Schizophrenia in the Male. A Psychiatric and Social Study Based on 138 Cases with Follow-up.** [Monograph, in English]
E. JOHANSON. *Acta psychiatrica et neurologica Scandinavica* [*Acta psychiat. (Khb.)*] **33**, Suppl. 125, 1–132, 1958. 4 figs., bibliography.

167. **Place of Methyl Phenidate Hydrochloride in Psychiatric Practice**
J. E. A. BARTLET. *British Medical Journal* [*Brit. med. J.*] **1**, 481–483, Feb. 21, 1959. 26 refs.

The author reports his experience with an 18-month trial of methyl phenidate (" ritalin ") in the treatment of psychiatric patients at Exminster Hospital, Devonshire. In a group of 26 patients with minor psychiatric disorders who were given methyl phenidate orally in doses up to 20 mg. twice daily, 10 out of 21 suffering from depression were completely relieved and a further 5 greatly improved. However, those with obsessional symptoms showed no improvement, and anxiety and hysteric or schizophrenic features tended to worsen. Severe endogenous depression was treated by modified electric convulsion therapy, but 3 atypical cases were treated by intravenous injection of methyl phenidate. One of these patients who was in a catatonic stupor did not respond, but the other 2 showed marked temporary relief from depression.

In a series of schizophrenic patients being treated with reserpine methyl phenidate was used to relieve the side-effects caused by the reserpine, these including restlessness, depression, fatiguability, and rigidity with tremor of an extrapyramidal type. Of 7 patients suffering from minor side-effects of reserpine and treated with methyl phenidate orally, the side-effects were completely relieved in all but 2; in these 2 depression, which had been manifest before reserpine treatment, persisted. In 11 cases treated by intravenous infusion of methyl phenidate the reserpine side-effects were completely relieved. Short case histories are given. In all cases, although the side-effects were relieved, psychotic symptoms of anxiety, behaviour disturbance, and schizophrenic thought were increased.

It is concluded that methyl phenidate has a place in the treatment of depression and in the relief of the side-effects of reserpine. *E. H. Johnson*

Dermatology

168. **Immunization against Superficial Fungous Infection. I. Studies on Experimental Animals**
E. L. KEENEY and M. HUPPERT. *Journal of Investigative Dermatology* [*J. invest. Derm.*] **32**, 7–13, Jan., 1959. 17 refs.

Experimental work on the immunization of animals against superficial fungus infection is reported. A vaccine was prepared from broth cultures of a strain of *Trichophyton mentagrophytes*, the aim being to destroy the fungus while extracting the antigens in, as nearly as possible, their native state. The dried vaccine was incorporated into " carbowax " and this preparation was rubbed into the skin of guinea-pigs daily for 6 weeks. Control guinea-pigs were treated with carbowax alone. Both groups of animals were then experimentally infected by topical application of cultures of the homologous fungus. There was a distinct difference between the treated and control animals in the degree of infection. In the controls there were extensive spreading lesions, whereas in the treated animals only circumscribed areas of inflammation developed. It is suggested that the technique used in the preparation of the antigen may have a wider application. An unusual feature of the method was the complete sterilization of the dried fungus suspension by grinding in a ball mill. *G. W. Csonka*

169. **Immunization against Superficial Fungous Infection. II. Studies on Human Volunteer Subjects**
M. HUPPERT and E. L. KEENEY. *Journal of Investigative Dermatology* [*J. invest Derm.*] **32**, 15–19, Jan., 1959. 2 refs.

A vaccine from broth cultures of *Trichophyton mentagrophytes* was prepared by a technique designed to minimize destruction of antigenic material [see Abstract 168]. The fungus was grown for 6 weeks in liquid medium; the growth was then homogenized at 5° C., dried, and ground to a powder in a ball mill until the viability of the fungus had been destroyed. This powder was incorporated into " carbowax " and applied daily to the skin of the fourth toe-web of healthy human volunteers. For control purposes one group of subjects was treated with a similar preparation made from an *Alternaria* strain and one with carbowax alone. After 4 weeks of application the subjects were exposed to infection with cultures of *T. mentagrophytes*, which were kept in contact with the skin of the fourth toe-web for 2 days. Analysis of the results indicated that acquired resistance developed in those subjects treated with *T. mentagrophytes* antigen. *G. W. Csonka*

170. **Lipoid Dermato-arthritis (Reticulo-histiocytosis)**
A. LYELL and A. J. CARR. *British Journal of Dermatology* [*Brit. J. Derm.*] **71**, 12–21, Jan., 1959. 2 figs., 27 refs.

171. **Studies in Contact Dermatitis. III. Nail Varnish**
C. D. CALNAN and I. SARKANY. *Transactions of the St. John's Hospital Dermatological Society* [*Trans. St John's Hosp. derm. Soc.* (*Lond.*)] 1–11, No. 40, 1958. 40 refs.

Allergy to nail varnish has been reported to account for 19·6% of cases of cosmetic dermatitis. Nail varnish dermatitis involves not so much the nails as those areas of the face, particularly the eyelids, which are habitually touched by the varnished nail. The rash is rarely eczematous, but rather a scaly erythema. Nail varnish contains five major components—dye, solvent (organic acetate or toluene), foundation (nitrocellulose), plasticizer (dibutyl phthallate), and resin—the last of which, usually aryl sulphonamide-formaldehyde, produces the reaction.

The authors have seen 56 cases of this type during the past 5 years. In many cases it was found difficult to establish the diagnosis, and tests involving " omission of usage " were usually unsuccessful. However, contrary to the reported experience of others, it was found possible to confirm the diagnosis in all cases by means of a patch test with the undiluted varnish, the results being read at both 48 and 96 hours and erythema alone being accepted as indicating reactivity in some instances.

Allene Scott

172. **Studies in Contact Dermatitis. IV. Epoxy Resins**
C. D. CALNAN. *Transactions of the St. John's Hospital Dermatological Society* [*Trans. St John's Hosp. derm. Soc.* (*Lond.*)] 12–19, No. 40, 1958. 16 refs.

The epoxy resins (prepared by the reaction of epichlorhydrin with a polyhydric phenol) have assumed major importance as the basis of many cases of allergic contact dermatosis encountered in those industries in which they are extensively used, especially that of aircraft manufacture. An added hazard is provided by the hardeners, often polyamides, which are combined with the resin, while men who use epoxy resins are often in contact with other substances, such as organic solvents, glass cloth, and powdered mica, which can also act as primary irritants. As a result the type of dermatitis seen in such cases is seldom due to the effect of only one factor. The eruptions involve the exposed skin surfaces and the genitalia and usually consist of a scaly erythema. In the author's experience the best patch-test results with resin or hardener are obtained with a concentration of 1 or 2% in soft paraffin. Of 20 men with dermatitis examined in an aircraft factory, 12 reacted positively to patch tests, 10 being allergic to the resin only, one to the hardener only, and one to both.

Allene Scott

173. **On Sudden or Rapid Whitening of the Hair**
A. J. EPHRAIM. *A.M.A. Archives of Dermatology* [*A.M.A. Arch. Derm.*] **79**, 228–236, Feb., 1959. 4 figs., 42 refs.

Paediatrics

174. **Perinatal Pneumonia. A Retrospective Study**
F. A. LANGLEY and J. A. McC. SMITH. *Journal of Obstetrics and Gynaecology of the British Empire* [*J. Obstet. Gynaec. Brit. Emp.*] **66**, 12–25, Feb., 1959. 7 figs., 19 refs.

The authors have studied the 87 cases of pneumonia occurring among 494 stillborn foetuses and newborn infants examined post mortem at St. Mary's Hospitals, Manchester, in the years 1950, 1952, and 1954, in an attempt to determine the causes of such infection and its role as a cause of perinatal death. They define perinatal death as "stillbirth or death in the first week of life" and pneumonia as "the presence of polymorphonuclear leucocytes in the air spaces or interstitial tissue of the lungs in more than minimal amounts". (In all cases of perinatal death examined post mortem at these hospitals sections from each lung are examined microscopically as a routine.) Analysis of the frequency of pneumonia in the whole series of necropsies according to age at death showed that whereas evidence of pneumonia was present in 10% of stillborn foetuses, it occurred in 25% of infants dying on the first day and in 30% of those dying on the second day; thereafter it was of less relative importance.

On the basis of their findings in this series the authors divide perinatal pneumonia into three types: (1) foetal pneumonia found in stillborn foetuses; (2) early perinatal pneumonia in infants dying during the first day; and (3) late perinatal pneumonia in infants dying in the first week but after the first day. Type 1 tends to occur in infants at or near term and Type 3 in premature infants. These types of pneumonia may also be defined in terms of maternal age and parity, Type 1 being most frequently associated with primiparity and a maternal age of 20 to 24 and Type 3 with multiparity and a maternal age of 30 to 34.

Pneumonia may be observed in macerated as well as in non-macerated stillborn foetuses, but whether intra-uterine pneumonia is the cause of death in such macerated foetuses cannot be definitely stated. Anoxia is of importance in relation to foetal pneumonia, but not to the other types. Prolonged labour after rupture of the membranes is also important in the causation of foetal pneumonia, and inflammation of the foetal surface of the placenta is always present in pneumonia of the stillborn, indicating the importance of the transplacental route of infection in this type. In the other types it may be possible to tell from bacteriological studies whether the infection was acquired during birth or later from the attendants or from the environment. The constant association of placental inflammation and foetal pneumonia suggests that the control of placental infection by antibiotic therapy may play a part in the prevention of foetal pneumonia, together with the control of obstetric factors, such as premature rupture of the membranes. Prevention of perinatal pneumonia in liveborn infants depends on the prevention of prematurity as well as on the control of infection. *J. Browne Kutschbach*

175. **Acute Laryngo-tracheo-bronchitis. An Account of 122 Cases Studied in the Hospital for Sick Children, Toronto**
A. M. PEACH and E. ZAIMAN. *British Medical Journal* [*Brit. med. J.*] **1**, 416–419, Feb. 14, 1959. 7 refs.

The predisposing causes, clinical features, and treatment of acute laryngo-tracheo-bronchitis are discussed with reference to 122 cases (out of a larger number) seen at the Hospital for Sick Children, Toronto, during the winter months of 1952–3 and 1953–4. The condition was severe in 38 cases, in all of which tracheotomy was performed. The incidence was highest in children aged 12 to 23 months; only 12 patients were under one year of age, but in 6 of these tracheotomy was required.

In more than half the cases the onset of symptoms coincided with falling climatic temperature and humidity, and the drying effect of central heating in Canadian homes was thought to be important in precipitating obstructive symptoms. Provision of a cool, moist atmosphere, with adequate hydration and oxygenation, was therefore the first aim in treatment. Mild sedation and administration of antibiotics were other therapeutic measures, the patients being closely observed for signs of increasing anoxaemia. The indications for tracheotomy were a rising pulse rate, diminishing air entry, and increasing restlessness in spite of treatment. The operation was performed without delay on patients admitted with severe obstruction, cyanosis, and peripheral collapse. The over-all mortality in this series was 0·8%, which compares very favourably with that in other reported series. *Margaret D. Baber*

176. **Faecal Incontinence and Encopresis in Childhood.** (Incontinentia alvi und Enkopresis im Kindesalter)
H. GÖTT. *Deutsche medizinische Wochenschrift* [*Dtsch. med. Wschr.*] **84**, 112–115, Jan. 16, 1959. 1 fig., 17 refs.

The author is of the opinion that the preoccupation of paediatricians during the past 30 years with behaviour disorders in dealing with faecal incontinence has caused other aetiological factors to be overlooked. He has recently seen 12 children with encopresis (one girl and 11 boys aged 5 to 13 years) at the University Children's Clinic, Bonn, and has been struck by the fact that although none of them had any neurological disease or local lesion of the rectum or anus, all had discarded the physiological maintenance of faecal continence by voluntary closure of the anal sphincter in favour of the inefficient technique of tight contraction of the glutei over the anal orifice. When these children were asked how they resisted a call to stool the older ones said "by pressing the buttocks close together, so that nothing can

happen ", and gluteal contraction was visible on demonstration in all cases. None of the children, when ordered to do so, was able to keep the sphincter closed, yet in all cases a strong reflex contraction was obtained when the anal area was stroked with a sound. The treatment adopted by the author was first to demonstrate the strength of the sphincter to the patients and to explain to him, fully and frankly, the cause of his incontinence. He then taught the patient how actively to contract the glutei and anal sphincter separately and stressed the importance of practising these two exercises frequently, especially when the desire to defaecate was experienced. Each child attended as an out-patient once or twice a week, when the progressive return of anal sphincter control was noted. All but one were discharged completely continent within 4 to 8 weeks. No adjuvant measures were necessary except those occasionally required to correct constipation. The one failure was with an illegitimate child whose mother would not cooperate in ensuring that the exercises were practised at home.

The author suggests that in cases of this type the child has tried to prevent an " accident " in some bygone emergency by tight contraction of the buttocks and has thereafter continued automatically to make use of a misdirected function, which has resulted in the incontinence he wished to avoid and of which he is usually deeply ashamed. Moreover, in " forgetting " how voluntarily to control the anal sphincter, he has become totally incapable of mastering his disability. The author claims his treatment to be effective for these encopretics without adjuvant measures, except, as stated, those required to correct constipation. *E. S. Wyder*

177. **Hirschsprung's Disease: Nine Years' Experience at the Hospital for Sick Children, Toronto**
B. LANGER and S. THOMSON. *Canadian Journal of Surgery* [*Canad. J. Surg.*] **2**, 123–130, Jan., 1959. 24 refs.

The authors first trace the steps leading to the formulation by Swenson in 1948 of the present concept of the pathogenesis of Hirschsprung's disease, of which the primary cause is now recognized to be a congenital maldevelopment of the innervation of the distal, undilated, segment of bowel. They then discuss the incidence and the clinical picture of the disease, both in its classic form and in the more recently recognized neonatal form, emphasizing that in either variety the final diagnosis must depend on biopsy of the mucosa or muscular wall of the rectum. The method developed by Swenson for the surgical removal of the aganglionic segment and restoration of continuity by anastomosis of the normal colon to the anus has replaced all other procedures in the treatment of the disease. A preliminary colostomy is recommended if the child is less than 12 to 18 months old or unfit to undergo the one-stage operation.

A review is then presented of the 58 cases of Hirschsprung's disease seen at the Hospital for Sick Children, Toronto, during the 9 years 1949–58, in 48 of which the patient was less than one year old on first admission, and 46 of which occurred in males. There were 20 deaths, though only 8 occurred after operation. The disease was confined to the recto-sigmoid in 47 cases, whereas in 4 it affected the whole colon and part of the small bowel. Of 14 cases in which intravenous pyelography was performed, only in one was dilatation of the bladder and ureter present; this disappeared after operation and was considered to have been due to external pressure from the dilated colon causing chronic obstruction.

Of 13 patients who received no treatment or were treated by medical or inappropriate surgical methods, 12 died, the diagnosis in 5 cases being first made at necropsy. Mikulicz's operation for resection of the dilated segment of the colon was performed on 11 patients in the early part of the period, with one death; symptoms recurred in 5 of the survivors and the procedure has now been abandoned as unsatisfactory. Of 15 patients treated by colostomy alone, 5 (3 of whom were moribund on admission) died; the remainder are awaiting admission for Swenson's operation when their condition permits. Out of 22 patients treated by Swenson's method (at ages ranging from one month to 11 years), only 2 have died. Of the remaining 20, the results in 11 are considered to be good and in 3 fair, while 6 have not yet been followed up for 6 months and the results cannot therefore be assessed. *Charles Nicholas*

178. **Obsessive-compulsive Neuroses in Children.** [In English]
E. G. REGNÉR. *Acta psychiatrica et neurologica Scandinavica* [*Acta psychiat. scand.*] **34**, 110–125, 1959. 8 refs.

Writing from the Children's Hospital, Göteborg, Sweden, the author discusses the way in which obsessive–compulsive symptoms and neuroses can arise in children. The well-known obsessions and ritualistic acts which are common in childhood are imitative in nature or result from collective agreement, whereas the neuroses have an individual personal pattern. Brain lesions can cause compulsive symptoms, and many tics are also obsessive–compulsive acts. Often the symptoms can be traced either to a particular or to a more general dread. In some cases altering the environment is enough to remove the origin of the fear. Obsessive thoughts and compulsive actions sometimes appear in children during a period of depression. Obsessive–compulsive symptoms do not represent a clinical entity, but they may be a stage in an anxiety–aggressive neurosis. Several case histories are presented to demonstrate that these symptoms can occur in children with widely varying environments and of different personality types. There is no definite association between an obsessive–compulsive neurosis and asthenia. Instances of apparent hereditary propensity are discussed, but the evidence is not conclusive.

The symptoms themselves are usually resistant to therapy, which must be directed to the underlying neurosis. This is considered to arise in most cases from some disturbance in the parent–child relationship, and the condition therefore requires careful therapy. The author is not convinced of the correctness of the Freudian concept that the symptoms disappear if their

meaning can be made clear to the patient. In some of his cases improvement in the general condition and disappearance of symptoms seemed to be quite unrelated to any understanding. The soothing of anxiety and relaxant drugs have a place in therapy, together with tonics in cases which appear after physically debilitating conditions. *E. H. Johnson*

179. **Mental Development of Children with Blindness Due to Retrolental Fibroplasia**
A. H. Parmelee, M. G. Cutsforth, and C. L. Jackson. *A.M.A. Journal of Diseases of Children* [*A.M.A. J. Dis. Child.*] **96**, 641–654, Dec., 1958. 23 refs.

The mental development of 38 children who were born blind as the result of retrolental fibroplasia was studied and compared with that of 22 children who were blind from other causes. The children were 5 to 9 years of age at the time of the study and some were at school. The medical history and details of progress at home and at school, which were obtained from parents and from the California School for the Blind and other education authorities in Los Angeles, were studied and the results of intelligence tests analysed. On the basis of the findings the children were classified as normal or mentally retarded (I.Q. less than 70).

Of the 38 children born blind as a result of retrolental fibroplasia, 12 were mentally retarded, compared with 9 of the 22 children who were blind from other causes; the difference was not statistically significant.
R. S. Illingworth

180. **The Effect of Maternal Thyroid Function on Fetal Thyroid Function and Development**
E. A. Carr, W. H. Beierwaltes, G. Raman, V. N. Dodson, J. Tanton, J. S. Betts, and R. A. Stambaugh. *Journal of Clinical Endocrinology and Metabolism* [*J. clin. Endocr.*] **19**, 1–18, Jan., 1959. 3 figs., 34 refs.

The authors of this paper from the University of Michigan, Ann Arbor, set out to answer the two questions: (1) whether maternal hypothyroidism could be the cause of foetal hypothyroidism, and (2) does sufficient thyroid hormone cross the placenta to ensure normal development of a foetus with primary hypothyroidism? As a first step the thyroid status of 17 women who had given birth to at least one cretinous child was assessed by clinical means and by investigations which included determination of the radioactive iodine uptake by the thyroid gland and serum protein-bound iodine (P.B.I.) and cholesterol levels. From the results it was concluded that 12 of these patients were euthyroid and 4 probably so, while the remaining patient was hypothyroid, but had received thyroid therapy throughout her two pregnancies, both of which had resulted in the birth of a cretinous child.

The effect of maternal thyroid function on the foetus was also studied in 14 pregnant bitches, of which 4 were euthyroid, 5 were made hypothyroid by means of thyroidectomy, and 5 hyperthyroid by administration of sodium L-thyroxine. Serial serum P.B.I. levels in the hypothyroid dogs were lower than in the euthyroid dogs at the time of delivery, but the thyroid function in living pups from the hypothyroid mothers was not significantly different from that of pups of euthyroid mothers. (These findings support reports in the literature that athyroid women can conceive and bear normal children even while they are myxoedematous.) It was noted that the pups of bitches made hyperthyroid with sodium L-thyroxine had a significantly higher serum P.B.I. level than had the pups of euthyroid and hypothyroid mothers, but the ratios of mean thyroid weight to mean body weight did not differ significantly. The histological appearances of the thyroid gland of pups born to hyperthyroid mothers were normal.

These results were similar to those in the infants of 2 of the human mothers investigated as described above who, when again pregnant, were treated with desiccated thyroid, and confirm that significant transplacental passage of thyroid hormone can occur. The clinical appearance, bone maturation, serum P.B.I. levels, and uptake of radioactive iodine by the thyroid gland were normal in both these infants at birth, but one was shown subsequently to be athyrotic. *R. M. Todd*

181. **Exophthalmic Goiter in Children**
A. B. Hayles, R. L. J. Kennedy, O. H. Beahrs, and L. B. Woolner. *Journal of Clinical Endocrinology and Metabolism* [*J. clin. Endocr.*] **19**, 138–151, Jan., 1959. 2 figs., 12 refs.

Over the 48-year period 1908 to 1955 217 girls and 36 boys with exophthalmic goitre were seen at the Mayo Clinic. The condition was diagnosed from the clinical history, the findings on physical examination, the protein-bound iodine level in the blood, and the basal metabolic rate. The patients fell into three groups, according to the type of treatment given. Group 1 (38 patients) were not subjected to operation at the Clinic, but 11 of the patients were treated surgically elsewhere, 2 of whom died. Treatment in the remaining 27 varied; it included administration of propylthiouracil in 3 and of iodides with reduction of activity in 14. In Group 2 (19 patients) treatment was by ligation of thyroid vessels or injection of sclerosing substances into the thyroid gland; there were 4 deaths in this group. In Group 3 (196 patients) subtotal thyroidectomy was carried out, preceded in 25 instances by ligation of the thyroid vessels. There were 4 postoperative deaths from pulmonary oedema (all before 1933). Follow-up examination of the patients in this group showed that hyperthyroidism recurred in 28 and further treatment was required; myxoedema developed in 49 patients, hypoparathyroidism in 2, paralysis of a vocal cord in one, and keloid formation in the operative scar in 7. Growth at adolescence was unaffected by subtotal thyroidectomy, but in 22 patients some degree of exophthalmos was still present.

Diabetes mellitus was present in 3 boys and 6 girls in this series; it preceded the onset of thyrotoxicosis in 4 patients and appeared 6 months to 10 years afterwards in 5. The authors state that the incidence of diabetes was higher than would be expected by chance occurrence.
R. M. Todd

Public Health

182. **Social Patterns of Road Accidents to Children. Some Characteristics of Vulnerable Families**
E. M. Backett and A. M. Johnston. *British Medical Journal* [*Brit. med. J.*] **1**, 409–413, Feb. 14, 1959. 11 refs.

A comparative study is reported of the family and social characteristics of two groups, each of 250 school-children, one of which had been involved in road accidents and the other had not. There has been little research into this problem, although one-third of all accidental deaths in children are due to road accidents. Among the various factors considered were family size, social and economic environment, protected and unprotected play, and maternal preoccupation.

The interaction of the various factors made it impossible to draw any definite conclusions, although certain circumstances seemed to increase the likelihood of accident. Illness, maternal or otherwise in the home, appeared to be a predisposing factor, other factors being maternal preoccupation with pregnancy and an excess of dependants per earner in the family. The families of children who had accidents were more crowded and protection during play was lacking, as were elementary play facilities. Intelligence of the child, a history of other accidents in the family, age structure of the family, and sibship size did not appear to be significant factors.

J. G. Jamieson

183. **Type-1 Poliovirus Isolated from a Budgerigar**
R. G. Sommerville. *Lancet* [*Lancet*] **1**, 495–496, March 7, 1959. 5 refs.

At the Virus Laboratory, Ruchill Hospital, Glasgow, a strain of Type-1 poliomyelitis virus was isolated on three occasions from a budgerigar which was recovering from an acute attack of paralysis of the legs. At the same time an apparently identical virus was found in the stool of a close contact of the bird, a 10-year-old boy in whom bulbar poliomyelitis developed which proved fatal. The isolation of the virus from an avian host was considered to justify the studies described in this paper.

A virus was isolated from the intestinal contents collected from the budgerigar post mortem and its cytopathic reactions were studied in various tissue cultures. For a number of reasons (which the author gives) the possibility of accidental contamination being responsible for what appeared to be a truly "avian" strain, was excluded. The virus was inoculated by various routes into 6 female budgerigars, but no paralysis developed although the birds suddenly ceased "chattering" and seemed otherwise unwell 14 days after the inoculation. No virus was recovered from the faeces of the birds, which were observed for 3 weeks and then killed. No abnormalities were found post mortem. Uninoculated control budgerigars kept in the next room maintained a constant "chatter" during the time the 6 inoculated birds were silent. Twelve 2-day-old chicks were experimentally inoculated with the same "avian" virus and some were given simultaneously an injection of hydrocortisone; none showed any effect.

A questionary was sent to the parents of 273 children who had had paralytic or non-paralytic poliomyelitis and from whom stool specimens had been examined for virus content at the laboratory during 1956 and 1957. Replies were received from 124 families, and 56 of these kept a pet budgerigar. In 17 of the 56 households the bird died at about the same time as the child contracted paralytic or non-paralytic poliomyelitis. *J. Cauchi*

184. **Budgerigars and Poliomyelitis**
D. S. Dane, G. W. A. Dick, and S. N. Donaldson. *Lancet* [*Lancet*] **1**, 497–498, March 7, 1959. 5 refs.

In Belfast during 1957 there were some 200 cases of acute poliomyelitis and aseptic meningitis, mostly due to Type-1 poliomyelitis virus, in children under 6 years of age. Of 73 patients with paralytic poliomyelitis, 24 kept pet budgerigars, and of 26 with the non-paralytic form, 6 did so. In 4 of these cases one or two birds died about the time of the patient's illness.

Using a total of 50 budgerigars the authors experimented with 11 different strains of poliomyelitis virus, each strain being fed to 3 birds which were kept in the same cage. On the 30th day after this feeding the birds were inoculated intracerebrally with the same virus, which was then looked for in the droppings; it was isolated only from the pooled faeces of one group of three birds which had been fed with a Mahoney laboratory strain of Type-1 virus. Since the virus was recovered on the first and second days after feeding and at no other time this was evidently no more than a passive excretion. Blood samples from each of these birds were examined before virus feeding, at the time of intracerebral inoculation, and one month later. At the final examination 2 of the 3 birds with virus in the faeces were found to have developed low-titre (1:10) neutralizing antibody to the type of poliomyelitis virus fed to them.

Five allegedly paralysed birds received from local breeders were examined. A past bone fracture was found in 4 and a large renal tumour involving the sciatic nerve in one. Blood samples taken from these 5 birds showed no neutralizing antibody to any of the three types of virus.

It is concluded that this investigation failed to demonstrate that budgerigars are commonly infected with poliomyelitis virus in Northern Ireland, although the possibility that these birds may occasionally become infected by a human excreter and later carry the infection to other human contacts cannot be ruled out.

J. Cauchi

Industrial Medicine

185. **Investigations Concerning the Pre-radiological Stage of Silicosis**
C. VELICAN, G. LATIS, M. POPA, G. POPA, and M. STEINBACH. *British Journal of Industrial Medicine* [*Brit. J. industr. Med.*] **16**, 40–42, Jan., 1959. 9 refs.

In an attempt to show that there is an evolutional stage of silicosis preceding the onset of radiologically demonstrable pulmonary lesions the authors have investigated at 6-monthly intervals 22 gold-miners during their first 2 years in the Rumanian gold mines. In the dustiest part of the mine, where the rock was of volcanic origin, the number of dust particles varied between 8,000 and 45,000 per ml. and 10% of the total weight of dust was in particles measuring less than 1 μ in diameter, while 50 to 68% consisted of particles of between 1 and 3 μ in diameter. The seams were formed for the most part of auriferous quartz and of iron and lead sulphides, the proportion of free and combined silica in these seams being about 72%. The 6 men working in this part of the mine showed a progressive increase of the blood silica level from 0·24 mg. to 0·91 mg. per 100 ml. At the same time the erythrocyte count fell from 4,000,000 to 3,500,000 per c. mm. and the haemoglobin value from 87% to 70%, while the eosinophil count rose from 1·5 to 4·8% and the monocyte count from 7·8% to 12·8%. Similar changes occurred, but were not statistically significant, in the other 16 miners who were exposed to smaller concentrations of dust.

The authors suggest that these changes represent the humoral phase of silicosis, which begins during the second year of exposure to dust and precedes by 3 to 7 years the radiological phase of pulmonary localizations. They consider the changes to be due to the toxic influence of the increased concentration of silica in the blood. Clinical symptoms include asthenia, adynamism, and anorexia.

Kenneth M. A. Perry

186. **The Topographic Distribution of Mineral Dusts in Some Pneumoconiotic Lungs**
P. GROSS and K. W. SMITH. *Diseases of the Chest* [*Dis. Chest*] **35**, 140–154, Feb., 1959. 27 figs., 6 refs.

Systematic study of the sites of deposition of mineral dust in pneumoconiotic lung tissue may ultimately provide a valuable contribution to our knowledge of the pathogenesis of dust disease of the lungs, and this aspect of pneumoconiosis has been investigated by a special photographic technique at the Industrial Hygiene Foundation, Mellon Institute, Pittsburg. For this purpose serial sections of lung tissue were stained for collagen and iron and special fields then selected for study, their location being fixed by a "field finder". These fields were first photographed and thereafter the sections were incinerated and the acid-soluble ash removed by immersion in hydrochloric acid. The same fields were then re-photographed under dark-ground illumination and the two negatives superimposed for comparison. Sections from five different types of case were intensively studied by this technique, these cases being (1) silicosis with slight asbestosis; (2) pure silicosis; (3) silicotuberculosis with slight asbestosis; (4) diatomite pneumoconiosis; and (5) asbestosis. The findings in each case are described and illustrated.

The authors suggest that the progressive character of silicosis is due to the transport of silica from the site of deposition to new locations, at which fresh inflammatory reactions are then initiated. This transport is demonstrated in old hyaline nodules which exhibit a peripheral "reactive" zone of younger, cellular, inflammatory tissue in which mineral dust particles are heavily concentrated. Another striking indication of how the transport of mineral dust may lead to the development of new inflammatory foci was revealed by the demonstration of infiltration of heavy mineral dust into previously uninvolved parenchyma adjacent to silica nodules. The non-progressive character of asbestosis is explained by the paucity of mineral in asbestotic scar tissue and by the difficulty of mobilizing and transporting asbestos fibres through the lattice of stromal fibrils. Among the other matters discussed are the significance of rounded versus stellate nodules, and of laminated versus non-laminated silicotic nodules. The authors observed that areas of tuberculous caseous necrosis, though occurring in the midst of silicotic tissue, were free from demonstrable mineral dust particles. In cases of silicosis of crystobalite type (Type 4 above) mineral dust was observed infiltrating not only the perivascular tissues, but also the vessel walls.

A. Meiklejohn

187. **Hygienic Aspects of Dust in Cement Factories.** (Сравнительная гигиеническая оценка пылевого фактора заводов, изготовляющих различные виды цемента)
N. SADKOVSKAJA. *Гигиена Труда и Профессиональные Заболевания* [*Gig. Truda prof. Zabolev.*] **3**, 39–44, Jan.–Feb., 1959. 3 figs., 10 refs.

In view of the difference of opinion as to whether the inhalation of cement dust can cause pneumoconiosis the author has investigated: (1) the differences between hygienic conditions at different cement works and the effect, if any, of these on the incidence of industrial disease among the workers; and (2) the changes produced in the lungs of experimental animals by inhalation of dust of the type occurring in cement factories.

The investigations at the factories showed that the dustiest conditions occurred where packing, storage, and non-mechanized handling of the dry powdered cement were carried out. The packers were exposed to a dust concentration which varied from 242 to 567 mg. per c. metre, and the charge hands to one of 283 to 545 mg. per c. metre. Between 44 and 98% of the dust particles

were less than 4 μ in diameter. The proportion of free silica in the dust varied between 3·1% during the manufacture of Portland-type cement and 67% during the manufacture of acid-resisting cement. Chest radiography of 261 cement workers, all having roughly the same duration of exposure, but to different types of dust, showed that pneumoconiosis developed earlier in those employed in making the acid-resisting cement.

In the animal experiments white rats were given intratracheal injections of 50 mg. of two kinds of cement dust with a free silica content of either 1 to 3% or 10 to 40% and kept under observation for 18 months. Rats exposed to the former dust did not develop typical silicotic nodules, but they did show numerous small miliary granulomata composed of lymphoid and epithelioid cells and occasional foreign-body giant cells identical with those found in workers exposed to talc. There was no sclerosis present in these lesions, although there was a moderate degree of peribronchial and perivascular sclerosis, with emphysema. The regional lymphatic nodes were similarly affected. In the rats given injections of marl dust containing 40% of free silica and 40% of combined silica a typical nodular silicosis developed.

It is suggested that the maximum allowable concentration of dust in the crushing and packing sheds of factories engaged in making acid-resisting cement should be 2 mg. per c. metre and elsewhere in cement factories it should be 10 mg. per c. metre. *Basil Haigh*

188. **The Diagnosis of Cancer of the Lung in Patients with Pulmonary Fibrosis of Toxic Origin.** (К вопросу о диагностике рака легкого у больных токсическими пневмосклерозами)
S. I. Ašbel'. *Гигиена Труда и Профессиональные Заболевания* [*Gig. Truda prof. Zabolev.*] **3**, 11–16, Jan.–Feb., 1959. 26 refs.

In this study the author appraises the value of the various methods of diagnosis of cancer of the lung in patients already suffering from established pulmonary fibrosis resulting from occupational exposure to toxic fumes or chemicals. Records of the Gorkii Institute of Occupational Hygiene show that the incidence of lung cancer is 1½ times greater among such patients than among those with non-occupational pulmonary fibrosis, and that the highest incidence is in patients aged between 40 and 60 years. The neoplasm appeared not less than 8 years, and usually 10 years, after the onset of the toxic fibrosis.

In the author's series of 14 cases only one could be treated surgically, the others being inoperable on account of cardio-respiratory or respiratory failure. Because cancer affects the prognosis adversely it is important that it should be diagnosed early. The difficulty in this is that the early symptoms are identical with those of pulmonary fibrosis, namely, cough, sputum, haemoptysis, pain in the chest, dyspnoea, weakness, wasting, and sometimes pyrexia. Both conditions are liable to be followed by focal pneumonia. Cytological examination of the sputum was found to be unreliable, for in only 3 cases were atypical cells suggestive of carcinoma found. Bronchography after injection of iodized oil is of great value in the early diagnosis of lung cancer, but it aggravates the condition of a patient with pulmonary fibrosis to such an extent that it is contraindicated. Radiologically the use of over-exposed, penetrating films may compensate to some extent for the inability to perform bronchography. The recently introduced method of tomo-fluorography is in the author's view very promising. Although bronchoscopy is in general well tolerated by patients with pulmonary fibrosis this is not so in regard to such patients in whom carcinoma is suspected as well, and in these cases is indeed usually contraindicated. The author concludes that, as in any other situation, there is no one reliable method of diagnosis of lung cancer in these patients, and all available methods must be used in combination. *Basil Haigh*

189. **Experience with Sodium Calciumedetate in Chronic Exposure to Lead.** (Unsere Erfahrungen mit $CaNa_2$ E.D.T.A. (Mosatil-Bayer) bei chronischer Blei-Exposition)
M. Savićević, L. Petrović, M. Stanković, and S. Djordjević. *Zentralblatt für Arbeitsmedizin und Arbeitsschutz* [*Zbl. Arbeitsmed.*] **9**, 6–12, Jan., 1959. 3 figs., 20 refs.

The effects of sodium calciumedetate have been studied at the Institute of Hygiene, Belgrade, in 30 workmen who had been employed for 5 to 16 years in the production and refining of lead. All of them showed various degrees of chronic lead poisoning and were under treatment at the local health centre. They were divided into 4 groups, all of which were treated with sodium calciumedetate for 7 days as follows: (I) daily intravenous infusion of 10 ml. of a 24% solution of the agent (11 cases); (II) 10 ml. of a 12% solution daily intravenously (5 cases); (III) 10 ml. of a 12% solution daily intramuscularly (7 cases); and (IV) two tablets each containing 0·5 g. of the sodium calcium-edetate given 3 times a day orally. A fifth group of 4 cases did not receive the drug and served as a control. All the subjects were given a good diet and kept at rest. Blood counts and haemoglobin estimations were carried out at the beginning and the end of the 7 days' treatment.

The blood lead levels decreased in all the groups, including the controls. Lead excretion in the urine was determined daily on 24-hour collections of urine, using a modification of the polarographic method of Baker. The urine coproporphyrin content, which was also estimated daily by the spectrophotometric method of Rimington, decreased during the course of treatment. The intravenous administration of the drug was the most effective route in promoting mobilization and excretion of lead, which reached a peak 6 hours after the beginning of treatment. However, the lead excretion levels in the urine remained higher than normal even after the 7 days' course of treatment, suggesting that this period is not quite sufficient.

The results confirm the evidence of other workers that sodium calciumedetate is a valuable drug for the treatment of lead poisoning. The authors point out that good food and rest contributed to the improvement which occurred in the control group. *R. Schoental*

Forensic Medicine and Toxicology

190. **Student Suicides**
A. ROOK. *British Medical Journal* [*Brit. med. J.*] **1**, 599–603, March 7, 1959. 11 refs.

The author, from the Department of Ecology, University of Cambridge, reports a study of the incidence of suicide among University students. Since the end of the Second World War student health services have been established at almost all British universities, and the work of these has revealed a high incidence of mental illness. Although these illnesses are often trivial, they have curtailed some university careers and on occasions have led to suicide, which was second only to accident as a cause of student deaths during the period 1948–58. At Cambridge University there were 14 suicides during that period, an annual rate of 21·3 per 100,000 living, compared with a rate (over a 9-year period) of 4·1 per 100,000 living (aged 20 to 24 years) in the general population. Since the actual number of suicides was small, the author emphasizes the danger of drawing erroneous conclusions from statistical tables. There were 3 suicides in coloured students at Cambridge during the period, which, on the basis of some 350 such students in residence in an average year, gave a very high incidence—namely, 85·7 per annum per 100,000 living. This figure, the author points out, " must be regarded with suspicion " in view of the small number of suicides that occurred. The only constant precipitating factor appeared to be worry over work.

Analysis of undergraduate deaths at Cambridge since 1928 showed that the annual suicide rate per 100,000 living was similar in the decade 1928–38 to that in the period under review, the rate in the decade 1938–48 being higher.

The author discusses methods of selection of university entrants and the effects of transition from schoolboy to student. He suggests that the intellectual freedom may induce a sense of loss of direction and inadequacy in weaker characters. The lack of information on factors which may lead to suicide and the need for more research into mental health problems are emphasized. Examinations are considered to have a significant influence on the incidence of suicide in undergraduates.

Gavin Thurston

191. **Disturbances of Acid–Base Equilibrium in Salicylate Intoxication**
R. W. WINTERS, J. S. WHITE, M. C. HUGHES, and N. K. ORDWAY. *Pediatrics* [*Pediatrics*] **23**, 260–285, Feb., 1959. 10 figs., bibliography.

Disturbances of acid–base equilibrium in salicylate intoxication were studied in 33 patients, most of whom were children who had received excessive doses of aspirin. In general there was a fall in the plasma CO_2 content, but the changes in the *p*H of the blood were not consistent. In 2 patients with an acid blood *p*H pulmonary oedema developed; one died, but the other recovered after prolonged artificial respiration. A less severe acidosis was present in those cases in which ingestion of the salicylate had started more than 24 hours earlier.

The acid–base disturbance was due to several factors, but chiefly to the accumulation of fixed anions, including chloride and salicylate, and of some undetermined anion believed to be ketone bodies. Treatment of the acidotic patients consisted in administration of water, chloride, sodium, potassium, and carbohydrate, but not bicarbonate or lactate. *V. J. Woolley*

192. **Evaluation of the Efficacy of Lavage and Induced Emesis in Treatment of Salicylate Poisoning**
F. J. ARNOLD, J. B. HODGES, and R. A. BARTA. *Pediatrics* [*Pediatrics*] **23**, 286–301, Feb., 1959. 6 figs., 3 refs.

The relative efficacy of gastric lavage and induced emesis in the treatment of experimental salicylate poisoning was studied at the Western Reserve University School of Medicine, Cleveland, Ohio. Fasting dogs were given 0·5 g. of sodium salicylate per kg. body weight, and at varying intervals thereafter gastric lavage (in some instances gastric aspiration) was carried out or vomiting was induced. It was found that in the recovery of ingested salicylate aspiration before the introduction of fluid was as effective as lavage, lavage within 15 minutes of ingestion was no more effective than emesis induced within 30 minutes, and lavage carried out after 60 minutes was almost valueless. Spontaneous vomiting was not as effective as induced vomiting. A single large dose of ipecacuanha was the most satisfactory emetic. It is pointed out that the introduction of fluid into the stomach is liable to promote passage of the stomach contents into the duodenum. *V. J. Woolley*

193. **Thrombocytopenia during Chlorothiazide Treatment**
P. NORDQVIST, G. CRAMÉR, and P. BJÖRNTORP. *Lancet* [*Lancet*] **1**, 271–272, Feb. 7, 1959. 1 fig., 9 refs.

Over a recent 12-month period at Sahlgren's Hospital, Gothenburg, chlorothiazide was given to about 400 patients, usually in a dosage of 1 g. daily. In 6 of them there was a severe fall in the blood platelet count and in 3 a purpuric rash also developed. The platelet count fell to about 20,000 per c.mm. and returned to normal when chlorothiazide was withdrawn. The addition *in vitro* of chlorothiazide to the blood of these patients caused platelet lysis in one case. In another case application of chlorothiazide to the skin caused a blister and infiltration. *V. J. Woolley*

194. **The Hemolytic Effect of Primaquine and Related Compounds: a Review**
E. BEUTLER. *Blood* [*Blood*] **14**, 103–139, Feb., 1959. 9 figs., bibliography.

Anaesthetics

195. **The Use of an Antigravity Suit in Neurosurgery**
I. P. FREUCHEN. *Acta anaesthesiologica Scandinavica* [*Acta anaesth. scand.*] **3**, 17–23, 1959. 3 figs., 9 refs.

A report is presented from Rigshospitalet, Copenhagen, on the use of the "antigravity" (anti-*g*) suit to counteract the grave respiratory and circulatory changes arising during the performance of neurosurgical operations with the patient in the sitting position. The anti-*g* suit consists of a pair of long trousers fitted with inflatable bladders to compress the legs, the thighs, and the lower abdomen, and is shaped to allow the gluteal and genito-perineal regions and the knees to remain exposed.

After a brief review of four previous trials by other workers based on similar principles, the author describes his experience with the suit in 14 cases compared with 14 control cases. The operation in which the anti-*g* suit was used was for decompression of the trigeminal ganglion in 5 cases, for prolapse of an intervertebral disk in 5 (cervical in 2 and lumbar in 3), for a tumour of the cerebello-pontine angle in 3, and for a tumour of the cervical medulla in one. The anaesthetic record charts in 2 cases, in one of which the suit was used while in the other it was not, are reproduced. The operations were of similar length, but whereas the control subject had an acoustic tumour removed, the suit was employed during the removal of a prolapsed disk. The charts show marked contrasts in respect of changes in blood pressure and pulse rate, dosage of vasopressor drugs, and infusion volumes. During one operation the suit was deflated; this was followed by an immediate fall in blood pressure and a rise in pulse rate, both of which were as rapidly restored by re-inflation. In the first two trials an inflationary pressure of 60 mm. Hg was used, but this was progressively reduced and in the last 8 cases 25 mm. Hg was used and appeared to give optimum results.

[Although this preliminary communication covers too few cases for a full evaluation of the method to be made, the favourable findings, sound rationale, and simplicity of the technique clearly justify its further trial in an extended sphere.] *Michael Kerr*

196. **Cardiovascular Effects of Procaine and Lidocaine (Xylocaine) during General Anesthesia.** [In English]
J. R. KIMMEY and J. E. STEINHAUS. *Acta anaesthesiologica Scandinavica* [*Acta anaesth. scand.*] **3**, 9–15, 1959. 2 figs., 16 refs.

The cardiovascular effects of intravenous procaine and lidocaine were compared in two series of patients under nitrous-oxide–thiobarbiturate anesthesia. The arterial blood pressure and electrocardiogram of these patients were continuously monitored while standardized doses of 2·2 mg. per kg. and 1·1 mg. per kg. of the test drug were administered. It was found that procaine administration was followed by cardiovascular depression in 50% of the doses administered, while a blood pressure increase was noted following 47% of the lidocaine injections. The lack of vasomotor depression with the administration of lidocaine is advantageous when this agent is used to supplement general anesthesia.—[Authors' summary.]

197. **Succinylcholine Drip during Craniotomy**
K. HALL, M. BALDWIN, and F. NORRIS. *Anesthesiology* [*Anesthesiology*] **20**, 65–70, Jan.–Feb., 1959. 9 refs.

The authors describe from the National Institute of Neurological Diseases, Bethesda, Maryland, a method for use in performing neurosurgical procedures involving an intravenous succinylcholine drip whereby the opening and closing of the craniotomy wound can be carried out under general anaesthesia, but the patient can be awake and cooperative during studies of cortical localization. It is carefully explained to the patient beforehand that (1) he will be awake during part of the operation, but will feel no pain or discomfort; (2) that he will have a tube in his windpipe which will prevent his talking; (3) that his breathing will be done for him, that he should not try to help, and that he can signal for more air if he wants it; (4) that his arms will be only lightly restrained and that he can move his limbs within limits; and (5) that he will feel weak because of the succinylcholine.

In most of the authors' cases induction was by thiopentone or halothane, preceded by sedatives and followed by intubation, succinylcholine, and gas and oxygen. Local scalp anaesthesia was obtained with cinchocaine. The administration of nitrous oxide should be stopped about 15 minutes before the neurosurgeon is ready to begin cortical recordings, which are carried out only when full consciousness is regained. For the 13 patients in the present series the average total duration of anaesthesia was 5 hours. Electrocorticograms and cerebral localization studies were successful in every case (16 operations). As the patient cannot talk he is shown how to communicate by means of a simple code of hand signals. If the speech centre is likely to be involved the method is not used, local anaesthesia only being employed. *W. Stanley Sykes*

198. **Effects of Oxytocin on the Response to Suxamethonium**
R. J. H. HODGES, J. R. BENNETT, and M. E. TUNSTALL. *British Medical Journal* [*Brit. med. J.*] **1**, 413–416, Feb. 14, 1959. 4 figs., 14 refs.

It has now been established that the prolonged administration of depolarizing relaxants causes a rise in the threshold of the motor end-plates to these agents and an enhanced susceptibility to non-depolarizing agents. This change in response occurs particularly in the very young, in myasthenia gravis, and in the presence of fluid and electrolyte disturbances, and may account for the resistance and abnormal responses to the short-acting depolarizing relaxants which have frequently been reported. Similar abnormal reactions have also been reported

following the continuous infusion of oxytocin in obstetric patients, and 5 such cases are reported in this paper. Experimental evidence is also presented in support of the hypothesis that continuous infusion of oxytocin alters the sensitivity of the end-plate to depolarizing agents.

All the patients were given a sleep dose of thiopentone, intermittent intravenous injections of 50 mg. of suxamethonium, and nitrous oxide and oxygen through an endotracheal tube without carbon dioxide absorption. Respiration was controlled. In each case artificial rupture of the membranes was performed followed by the infusion of oxytocin to induce labour. In the first case a mid-cavity forceps delivery was performed, during which 3 doses of suxamethonium were given, the last of which produced a curarizing effect which lasted 30 minutes and was then reversed with atropine and neostigmine. In the other 4 cases induction failed and caesarean section was performed; these patients also remained curarized for varying periods after the last dose of suxamethonium.

To determine the part played by oxytocin in producing these abnormal reactions 6 patients were lightly anaesthetized with a sleep dose of thiopentone followed by nitrous oxide and oxygen, and the respiratory depressant effects of two doses of 20 mg. of suxamethonium given intravenously, one before and the other after one to 4 hours' continuous infusion of oxytocin, were observed by means of a kymograph or a continuously recording spirometer. The second dose of suxamethonium produced no muscle fasciculations, nor was the duration of apnoea significantly longer than after the first dose, but the total duration of respiratory depression was increased by about 50%. The difference in effect of the two test doses of suxamethonium was similar to that observed before and after the induction of end-plate resistance by the prolonged administration of depolarizing agents.

The authors conclude that the intravenous infusion of oxytocin modifies the action of suxamethonium. Fasciculations are minimal or absent and normal doses of the relaxant do not produce apnoea, but a non-depolarizing type of neuromuscular block occurs which is slower in onset than a depolarizing block and the duration of total respiratory depression is prolonged. Recovery may be speeded up with neostigmine. *M. Woods*

199. **Anesthesia in Relation to Electroshock Therapy**
R. J. M. STEVEN and R. M. TOVELL. *Anesthesia and Analgesia; Current Researches* [*Anesth. Analg. curr. Res.*] **38**, 42–49, Jan.–Feb., 1959. 2 figs., 5 refs.

The authors describe the method of anaesthesia used at Hartford Hospital, Connecticut, to produce muscular relaxation in patients about to undergo electric convulsion therapy (E.C.T.). In all cases E.C.T. was carried out in the morning with the patient in the fasting state; no premedication was given. The method of anaesthesia was as follows. An intravenous injection of 100 to 250 mg. of thiopentone was administered, and as soon as the patient was asleep 20 to 100 mg. of suxamethonium was injected. Oxygen was administered by bag and mask during the period of muscular fasciculations. A rubber gag was placed between the teeth and the shock then given. Inflation of the lungs with oxygen was resumed during the clonic convulsive phase and continued until adequate spontaneous respiration returned. This method was used for a total of 14,870 treatments given over the 5-year period 1953–57 to patients aged 13 to 87 years. Prolonged apnoea was not observed in any of the cases. There was one death in the series, that of an elderly man who, after injection of suxamethonium, vomited copiously and died from pulmonary complications. In one case mild pneumonia developed following aspiration of vomitus. *Mark Swerdlow*

200. **Nitrous Oxide Anaesthesia for Bronchoscopy. A Method Suitable for Out-patients**
D. BROWN and J. V. I. YOUNG. *British Medical Journal* [*Brit. med. J.*] **1**, 692–695, March 14, 1959. 15 refs.

A method of anaesthesia with nitrous oxide which is suitable for the performance of bronchoscopy on out-patients and is based on 723 bronchoscopies carried out mainly on such patients is described. The procedure is as follows. The patient's state of fitness is assessed. Superior vena caval obstruction is regarded as an absolute contraindication, since the action of intravenous drugs may be delayed, and cardiovascular disease as a relative contraindication. The rejection rate in the present series was only 2%. The patients are told that they will be in a dream-like state but not that they will go right off to sleep; the authors warn that an occasional patient may hear and recall what has been said during bronchoscopy. Adult patients are given 1/75 grain (0·8 mg.) of atropine sulphate intramuscularly one hour preoperatively. The gas machine flowmeters are set to deliver 5 litres of oxygen and 10 litres of nitrous oxide a minute, which the patient breathes from a mask, and then 1 ml. of 2·5% thiopentone solution for each 28 lb. (0·08 ml. per kg.) body weight is injected intravenously through a Gordh needle; this solution also contains 1·5 mg. of gallamine triethiodide per ml. to prevent muscle fasciculations. When this has acted, suxamethonium chloride in a dose of 5 mg. per stone (0·8 mg. per kg.) body weight is given. When the breathing has stopped the lungs are ventilated with the nitrous oxide and oxygen mixture for 3 minutes in order to reduce the amount of nitrogen and carbon dioxide in the lungs, increase alveolar oxygen tension, and provide an effective concentration of nitrous oxide in the brain. The Negus bronchoscope is then passed quickly, with the gas mixture flowing through tubing attached to the nipple provided, apnoea being maintained with intermittent doses of suxamethonium and the chest compressed rhythmically with a Pinkerton cuirass to lessen the accumulation of carbon dioxide. If cyanosis occurs it is corrected immediately by passing the nitrous oxide and oxygen mixture directly down the lumen of the bronchoscope with a No. 8 Magill endotracheal tube. Additional oxygen may be added by using the by-pass. At the end of the procedure the bronchoscope is removed and the lungs are ventilated with the nitrous oxide and oxygen mixture through a mask until muscle power returns. The patient is then sat up and regains consciousness quickly, but is kept resting for at least one hour. Children are premedicated

with papaveratum and scopolamine, nitrous oxide and oxygen being used to induce anaesthesia and the intravenous needle being inserted while the child is asleep; children are not treated as out-patients.

The patients were of all ages and the duration of the procedure ranged from 3 to 30 minutes. Prolonged apnoea occurred only once; there were no fatalities. Suxamethonium given by itself was found to cause severe pain in the trunk and limbs in the first few days following the examination because of muscular fasciculation and gallamine was therefore added to the solution. Discussing the advantages of this method, the authors point out that topical anaesthesia causes considerable distress to the patient. As this is not an unavoidable necessity the present method using general anaesthesia was introduced. It does not increase the risk for the patient, hamper the operator, or cause more work for the nurses, and the patient has the use of all his protective reflexes at the end of the procedure. It is not, however, without its dangers and demands cooperation between all concerned and close attention to the finer points of technique. *M. Woods*

201. **Choice of Pressure-breathing Apparatus**
M. SAKLAD, E. SAKLAD, and C. V. COX. *Anesthesia and Analgesia; Current Researches [Anesth. Analg. curr. Res.]* **38**, 32–41, Jan.–Feb., 1959. 15 figs., 5 refs.

The intrapulmonary pressure patterns obtained with various pulmonary ventilators were studied at Rhode Island Hospital, Providence, R.I. Pressure changes inside a rigid 60-litre chamber connected via a variable resistance to a gas machine and to the respirator were recorded. Each ventilator tested was set to deliver 625 to 750 ml. per stroke and was allowed to function as a positive-pressure device only. Using this circuit the authors studied the pressure patterns obtained with four ventilators—those of Emerson, Jefferson, Bennett, and Stephenson. In addition they studied the effect of an interposed resistance on the pulmonary inflation achieved by the same respirators. Results are set out in diagrams and in tables. *Mark Swerdlow*

202. **Performance Characteristics of Vaporizers for Administration of Fluothane**
L. W. FABIAN, C. R. STEPHEN, M. BOURGEOIS-GAVARDIN, and S. J. DENT. *Anesthesiology [Anesthesiology]* **20**, 27–30, Jan.–Feb., 1959. 5 figs., 10 refs.

Writing from Duke University, Durham, N. Carolina, the authors enumerate the necessary characteristics of vaporizers to be used for the administration of "fluothane" (halothane), pointing out that such apparatus must be accurate and precise in view of the potency of this anaesthetic agent. In their experience the "fluotec" (cyprane) model fulfils most of the criteria. It is compensated for temperature changes and for changes in the rate of gas flow; its range varies from 0·5 to 3·0 volumes % and the concentrations can be altered by steps of 0·1%. The increases in gas flow over a range varying from 4 to 16 litres per minute are linear and regular. The Ohio (Heidbrink) vaporizer provides a range from 0·0 to 4·0 volumes % at a rate of gas flow of 4 litres per minute, but the increases are not so regular.

The F.N.S. vaporizer is simple and accurate and will fit Heidbrink, Foregger, and Boyle's machines. A graph has to be used for rates of gas flow other than 4 litres per minute. Lowering of the temperature as a result of evaporation causes lower concentrations to be delivered, except when the gas flow is small. Lastly the Foregger "copper kettle" and Heidbrink "vernitrol" vaporizers, which were not originally designed for halothane, deliver similar quantities for a given gas flow. Temperature compensation is provided for by the metals used in their construction. The flow from the vaporizer requires dilution by means of high gas flow rates to ensure safety. The authors emphasize that halothane can be safely given only when the vaporizer is placed between the flowmeter and the inlet to the rebreathing or circle system. It is concluded that the fluotec vaporizer most nearly approaches the ideal. *W. Stanley Sykes*

203. **Rectal Thiopental in New Dosage Forms: Multidose Suppositories or Suspension in "Abbosert"**
S. N. ALBERT, E. E. HENLEY, C. A. ALBERT, and H. N. ECCLESTON. *Anesthesia and Analgesia; Current Researches [Anesth. Analg. curr. Res.]* **38**, 56–60, Jan.–Feb., 1959. 3 refs.

Experience of two forms of rectal administration of thiopentone, multidose suppositories and a stable suspension which can be given rectally by means of a (disposable) plastic syringe, is reported in this paper from the District of Columbia General Hospital, Washington. Multidose thiopentone suppositories were given to 454 children aged 1 month to 12 years, the dosage being 1 g. per 50 lb. (44 mg. per kg.) body weight: the suppositories contained 1 g. of thiopentone per 5 cm. length. The rectal suspension was tried in 100 children, aged 2 weeks to 12 years, the dosage of thiopentone again being 1 g. per 50 lb. body weight. Judged by the completeness of the basal hypnosis produced, the suspension was as satisfactory as the suppositories. Experiments on rabbits showed that the medium in which the thiopentone was suspended did not irritate the rectum or modify the effects of the drug. *Mark Swerdlow*

204. **Pentothal Sodium: 1935–1957**
J. S. NIELSEN and W. E. SPOEREL. *Anesthesia and Analgesia; Current Researches [Anesth. Analg. curr. Res.]* **38**, 29–31, Jan.–Feb., 1959. 3 refs.

The anaesthetic effect of two batches of sodium thiopentone—one manufactured in 1935 and one in 1957—was compared. The drugs were in unlabelled ampoules and were administered intravenously to 17 albino rats in a dose of 30 mg. per kg. body weight. The time of return of various reflexes, including righting of the head, trunk, and limbs, and of locomotion was noted. There was no difference between the two samples in duration of effect or speed of recovery. Thiopentone manufactured in 1935 was given together with nitrous oxide and oxygen to 16 patients undergoing short operations; anaesthesia and recovery were uneventful.
Mark Swerdlow

Radiology

RADIODIAGNOSIS

205. **Suprasternal Transaortic Coronary Arteriography**
W. M. LEMMON, J. S. LEHMAN, and R. A. BOYER. *Circulation* [*Circulation*] **19**, 47–54, Jan., 1959. 6 figs., 13 refs.

Coronary arteriography by direct needle puncture of the ascending portion of the thoracic aorta was performed on 31 patients at the Hahnemann Medical College, Philadelphia. Transient electrocardiographic changes, such as sinus tachycardia, sinoauricular block, auricular or ventricular ectopic beats, or inversion of the T wave, occurred during 17 of the 35 examinations performed. The authors state that in no case to their knowledge did the needle puncture the aortic sinuses, the aortic valve, or the coronary arteries, but one patient developed a small pneumothorax. The majority of patients complained of some slight or moderate substernal discomfort which, however, seldom persisted for more than 24 hours.

The essential purpose of this investigation was to visualize the coronary arterial system (23 examinations). In 11 cases arteriography by this method was also used to determine the degree of aortic incompetence present, and in one patient it was used to demonstrate a suspected patent ductus arteriosus. In 12 of the cases it was in fact possible to compare the findings of coronary arteriography with those later obtained at cardiac surgery through direct inspection and digital examination of the coronary arteries. A good correlation between the radiological and surgical findings was established in 8 cases and a partial correlation in 4 cases.

[Although the transient electrocardiographic changes which occurred during arteriography are described, the authors make no mention of the initial electrocardiographic findings. It is thus not possible to correlate the coronary arteriographic and surgical findings—which are described in some detail in the 2 cases subjected to operation—with any abnormality which may have been present in the electrocardiogram.] *A. G. Freeman*

206. **Inhalation Radiocardiography**
C. H. JAIMET, R. H. TOMLINSON, and P. F. NACE. *Canadian Medical Association Journal* [*Canad. med. Ass. J.*] **79**, 972–977, Dec. 15, 1958. 6 figs., 4 refs.

The studies reported in this paper from St. Joseph's Hospital and McMaster University, Hamilton, Ontario, were concerned primarily with the investigation of the circulation in the left heart and myocardium by inhalation radiocardiography, a technique involving the inhalation of methyl iodide labelled with radioactive iodine (^{131}I) or of radioactive krypton (^{85}Kr). The labelled methyl iodide was prepared by simple exchange with labelled sodium iodide, separated, and dispensed into vials in a high-vacuum assembly. The labelled krypton was gas-pipetted in a vacuum system and adsorbed on charcoal in cooled vials. Both were administered by means of a respiratory mask connected to a hand-warmed tube wherein the vial was broken with a glass rod. The patient was instructed to inhale quickly and resume normal breathing rhythm at once. The dose of methyl iodide was 15 μc. and that of krypton 5 mc. Krypton has the advantages over methyl iodide of a long physical half-life, a very short biological half-life, and absence of selective concentration in any organ. Radioactivity was measured in the seated patient by directing a collimated scintillation crystal on the fourth thoracic interspace one inch (2·5 cm.) to the left of the sternum, the output being continuously recorded from a ratemeter with short integrating time. The log. counting rate was then plotted against time in seconds.

Typical curves obtained from normal subjects and patients with angina are reproduced. The normal curve is characterized by a sharp initial rise followed by a relatively quick fall to about half the peak value and then a more gradual fall, which can be followed for 40 seconds or more with krypton, but for only about 10 seconds with methyl iodide. Curves from patients with coronary disease show the same sharp initial rise, but the subsequent fall is more gradual. Careful analysis of the descending part of the curve obtained with krypton discloses that it shows two exponentials, the first of which is considered to represent the disappearance of activity from the cavity of the left heart and the second the rate of decay of activity from myocardium (though there is some doubt about the interpretation of this second part of the curve). It is claimed that the ratio of the intercepts of these two exponentials provides an indication (though not an absolute measurement) of the fraction of the cardiac output carried to the myocardium by the coronary circulation, low values (20%) being obtained from normal subjects and increasing values (55 to 80%) from patients with progressively more severe angina.

Brief mention is made of preliminary studies of the use of inhalation radiocardiography for the identification of valvular and congenital heart disease. It is suggested that the technique may be most useful clinically in the comparative study of heart function and of changes in response to specific therapy. *I. M. Rollo*

207. **Pulmonary Manifestations in Collagen Diseases**
C. M. NICE, A. N. K. MENON, and L. G. RIGLER. *American Journal of Roentgenology, Radium Therapy, and Nuclear Medicine* [*Amer. J. Roentgenol.*] **81**, 264–279, Feb., 1959. 12 figs., 39 refs.

The authors have reviewed the case records and radiographs of 109 patients admitted to the University of Minnesota Hospitals during the 15 years 1942–56 with collagen diseases. There were 40 cases of periarteritis nodosa, 37 of disseminated lupus erythematosus, 20 of

scleroderma, 7 of dermatomyositis, and 5 of rheumatic pneumonitis. In 75 cases the diagnosis was confirmed by means of necropsy or biopsy. Radiological abnormalities in the lungs, pleura, or heart were demonstrated in about two-thirds of the cases, and details of 12 of these are given to illustrate the principal abnormalities found and those combinations of x-ray features which may be of diagnostic significance.

The association of "interstitial pneumonitis" and pleural effusion is stated to be suggestive of collagenosis, and the addition of non-specific cardiac enlargement and prominent hilar shadows in the absence of peripheral pulmonary congestion makes the diagnosis even more likely. The presence of interstitial fibrosis and emphysema is similarly suggestive when confined to the lower and middle zones and accompanied by small, cyst-like changes, while the combination of these with non-specific cardiac enlargement, lack of peristalsis and widening of the oesophagus, and subcutaneous calcification is diagnostic of scleroderma. Pleural and pericardial effusions occurring together favour the diagnosis of disseminated lupus erythematosus or rheumatic pneumonitis, and hilar vascular prominence is a frequent finding in periarteritis nodosa. *D. E. Fletcher*

208. **A Self-retaining Catheter for Selective Bronchography.** (Управляемый катетер для бронхографии с надувной манжетой)
I. A. Goncov. *Вестник Рентгенологии и Радиологии* [*Vestn. Rentgenol. Radiol.*] **34**, 70–72, Jan.–Feb., 1959. 3 figs.

The author describes a most ingenious device by means of which bronchography of any major part of the bronchial tree can be carried out with the patient lying comfortably supine on the examination couch. Under radioscopic control the tip of the catheter can be pointed in any direction by means of a thread attached to its end so that by suitably manipulating the free end of the thread the operator can direct the end of the catheter into any chosen bronchus.

In addition the instrument is fitted with an inflatable rubber sleeve which surrounds the end of the catheter just above its terminal opening and which is connected to a suitable pump by means of a thin rubber tube. Once the tip of the catheter is located in the chosen bronchus the sleeve is inflated and thus occludes the bronchus and at the same time serves to immobilize the catheter. In this way it is possible to inject an upper-lobe bronchus without the risk of the contrast medium spreading to other parts of the bronchial tree. Also, at the end of the examination the contrast medium can be removed by aspiration with a syringe. *A. Orley*

209. **Opacifying Gallstones**
E. Salzman, R. P. Spurck, L. C. Kier, and D. H. Watkins. *Journal of the American Medical Association* [*J. Amer. med. Ass.*] **169**, 334–338, Jan. 24, 1959. 5 figs., 8 refs.

Certain types of gall-stone become radiologically opaque after prolonged exposure to suitable contrast media. In the study here described from the University of Colorado, Denver, "telepaque" (iopanoic acid) was given in a dose of 1 g. 3 times a day for 4 days to 123 patients in whom there was poor or no visualization of the gall-bladder after a single dose. Of 13 patients with pathologically proven stones in the bile ducts, 10 had stones which opacified. In 3 cases there was no opacification, either because extreme jaundice kept the concentration of dye too low, or because the stones were of the wrong type. In 9 of the patients in whom opacification eventually was obtained the serum bilirubin level was raised (up to 5 mg. per 100 ml.).

Experiments *in vitro* on 100 samples of biliary calculi removed either at operation or necropsy showed that about 20% opacified; all pure cholesterol or cholesterol-surfaced yellow stones associated with infection were non-opacifying, whereas all stones associated with bile-duct stasis (composed of a cholesterol core with a soft friable outside pigment zone) opacified. Pigment-surfaced stones from cases of infection could be either opacifying or non-opacifying. It is not clear whether opacification occurs *in vivo* with dyes other than iopanoic acid. Most of the tests *in vitro* were performed by adding various contrast media to normal bile in a concentration similar to that which occurs in taking a cholecystogram. [The more satisfactory method of obtaining bile at operation from a patient who had previously been given contrast medium was apparently used only once.] Further work is in progress. It is suggested that stasis leads to the oxidation of bilirubin and that the resultant biliverdin interacts with the contrast medium. *Denys Jennings*

210. **Diagnostic Value of Intravenous Cholangiography during Acute Cholecystitis and Acute Pancreatitis**
H. C. Johnson, B. D. Minor, J. A. Thompson, and H. S. Weens. *New England Journal of Medicine* [*New Engl. J. Med.*] **260**, 158–161, Jan. 22, 1959. 1 fig., 7 refs.

Since the differentiation of acute cholecystitis from acute pancreatitis is an urgent problem which can present considerable difficulty, the authors have investigated the value of intravenous cholangiography in making the differential diagnosis, arguing that in the performance of the intravenous cholangiogram the gall-bladder fills passively if there is no inflammation causing blocking of the cystic duct and therefore a normal appearance of the bile ducts and gall-bladder should reasonably exclude the presence of acute cholecystitis. Pancreatitis, on the other hand, should have no effect on the secretion of contrast medium from the liver and its passage into the duct system and into the gall-bladder.

At Grady Memorial Hospital (Emory University), Atlanta, Georgia, 61 patients in whom the clinical diagnosis pointed to one or other of these conditions were examined by intravenous cholangiography. The findings showed that of the 23 which later were reliably proved to be cases of acute pancreatitis, both the gall-bladder and ductal system were clearly outlined in 15 (65%); in none of these cases was the ductal system alone outlined, and in 8 (35%) there was no visualization at all. Of the 38 reliably proved cases of acute cholecystitis, the ductal system only was outlined in 18 (47%) and in no case was the gall-bladder visualized; in the remainder

of the cases in this group no visualization at all was obtained.

The authors conclude from these results that intravenous cholangiography can be most helpful in differentiating these two conditions: thus visualization of both the gall-bladder and ductal system points to acute pancreatitis, while visualization of the ductal system only points to acute cholecystitis. They note that in a fairly large minority of patients visualization of the biliary system does not occur at all and naturally in these cases no inference can be drawn. No false positive or false negative results were obtained in this series, although these can occur. *A. M. Rackow*

RADIOTHERAPY

211. **Total Thoracic Supervoltage Irradiation Followed by the Intravenous Infusion of Stored Autogenous Marrow**
K. A. NEWTON, J. G. HUMBLE, C. W. WILSON, D. E. PEGG, and M. E. G. SKINNER. *British Medical Journal* [*Brit. med. J.*] **1**, 531–535, Feb. 28, 1959. 5 figs., 15 refs.

The treatment of 2 patients with multiple pulmonary metastases by total thoracic irradiation at the Westminster Hospital, London, is described. The first patient had had an osteogenic sarcoma of the wrist treated by irradiation, resulting in recalcification, and the second patient had had a Ewing's tumour of the ischium, which had also been successfully treated with x rays. In both cases, however, multiple metastases had subsequently developed in the lungs. It was decided to treat the metastases with doses of the order of 3,000 r. to the whole chest in 2 weeks. Immediately before starting the irradiation bone marrow was aspirated from a number of sites in each case, sieved, and frozen. [The process is described in some detail.]

The first patient was treated partly at 2 MeV. and partly at 250 kV. by two opposed fields, there being considerable constitutional disturbance. A total maximum soft-tissue dose of 2,637 rads was given, the estimated integral dose being 39·4 megagramme-roentgens. Two days after the completion of treatment her stored bone marrow was infused intravenously. There was an immediate temporary rise in the total leucocyte count, which, it is postulated, was probably due to the stimulating action on the haematopoietic tissues of a non-cellular humoral factor in the marrow injection. This was followed by a slower progressive rise, and 13 days after the infusion there was " considerable evidence of marrow regeneration ". The patient died 3 months after treatment, radiographs of the chest having shown neither progression nor regression of the metastatic disease. The second patient was treated with 2-MeV. x rays only and received a maximum soft-tissue dose of 2,860 rads and an integral dose of 45·3 megagramme-roentgens. The treatment caused no constitutional disturbance and resulted in rapid and complete regression of the pulmonary metastases. After the infusion of bone marrow on the last day of treatment there was again an immediate temporary response followed by a steady and sustained rise in the leucocyte count indicating that regeneration was taking place. The patient has remained well since treatment was completed on Nov. 7, 1958, and there is no sign of recurrence.

The authors point out that the 2-MeV. Van de Graaff generator used in these cases has the advantages that its high output enables large fields to be used and that there is relatively small differential absorption in bone and soft tissue. The fields used were so shaped as to irradiate as little as possible tissue other than the lungs.

E. D. Jones

212. **Irradiation of the Entire Body and Marrow Transplantation: Some Observations and Comments**
E. D. THOMAS, H. L. LOCHTE, and J. W. FERREBEE. *Blood* [*Blood*] **14**, 1–23, Jan., 1959. 4 figs., 48 refs.

It has been shown experimentally in several species that the infusion of normal bone marrow enables an animal to survive exposure to degrees of irradiation that would otherwise prove fatal, but information concerning the applicability of this procedure to man is as yet scanty. The purpose of this paper from the Mary Imogene Bassett Hospital, Cooperstown, New York, and the Children's Medical Center, Boston, is to present further clinical experience with whole-body irradiation and marrow transplantation in man and to discuss some of the problems that arise.

Clinical details are given of 7 cases (with necropsy reports in 6) in which whole-body irradiation was carried out followed by intravenous infusion of bone marrow. In 3 of these there was some evidence that marrow transplantation had been successful, and one patient was reported to be well, with a normal haemoglobin level and total leucocyte count (though with 6% blast cells) on the 203rd day after completing irradiation. All but one of the patients were suffering from leukaemia, and no autogenous marrow infusions were given.

The general subject of whole-body irradiation and marrow transplantation is discussed in considerable detail. To enable marrow function to be re-established by means of marrow grafts the dose of radiation must be sufficiently high to reduce the reaction of the tissues to foreign marrow, and the whole body should receive as even a dosage as possible. In this connexion the advantages of using supervoltage irradiation are pointed out and it is suggested that the success with which marrow transplantation can be carried out in the mouse may be related to the ease with which an even dosage can be given to such an animal. But the immediate post-irradiation problem is the control of infection, and the leucocytes from successful marrow grafts will not in themselves provide adequate antibacterial defences. In addition the restoration of satisfactory lymphopoietic function in the lymph nodes and the spleen is needed, and the possible use for this purpose of transplants of immunologically immature foetal liver and spleen is discussed. *E. D. Jones*

213. **On Tolerance of Brain Tissue and Sensitivity of Brain Tumours to Irradiation.** [Monograph, in English]
M. LINDGREN. *Acta radiologica* [*Acta radiol. (Stockh.)*] Suppl. 170, 1–73, 1958. 30 figs., 42 refs.